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DEVELOPMENT AND TRAINING OF HIGHER ORDER COGNITIVE FUNCTIONS AND THEIR INTERRELATIONS

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Stockholm 2011

Published by Karolinska Institutet. Printed by Larserics Digital Print AB

ISBN 978-91-7457-247-6

ABSTRACT

Inhibitory functions (IFs) and working memory (WM) are essential for higher order cognitive functions such as non-verbal reasoning (NVR). WM is the ability to temporarily store and process information. IFs involve resisting automatic, inappropriate responses and limiting the interference of information held in WM. Deficits in them are associated with learning difficulties and Attention Deficit Hyperactivity Disorder. The behavioral link between IF and WM has been well established, whereas the neural correlates have not. Studies have shown that it is possible to train WM in school-aged children and adults and that effects can transfer to measures of IFs and NVR. Training efforts on IFs have been sparse, with no improvements on WM demonstrated. NVR training has mostly involved strategy learning and has not been reported in preschool children. The aims of the thesis were to study: the relation between WM and IFs (**Study I & II**), the effects of targeted cognitive training of either: WM (**Study II** & **IV**), IFs (**Study II**), NVR, or both WM and NVR (**Study IV**) on preschoolers and finally, the effects of musical practice on WM and NVR (**Study V**).

Study I reports that IFs and WM rely partly on activation of the same brain areas. Results showed an overlap in the right inferior frontal and, at a lower threshold, the right middle frontal gyrus and right parietal regions. **Study II** aimed to investigate whether training either IFs or WM would lead to improvements on the functions themselves and one another. This was studied in preschoolers, where individuals practiced either IFs or WM tasks 5 days/week for 5 weeks. The visuospatial WM training led to improvements on a verbal WM task and measures of sustained attention, whereas IF training led to improvements on trained tasks only. **Study III** aimed to increase the precision in which WM can be measured in low capacity individuals. This was done by testing 4- and 6-year-olds on multiple items of a WM span task, extracting the item difficulties, explaining their difficulty with logistic regression, and finally arranging selected items into sub-levels, thus increasing the possibility for further differentiation between abilities. **Study IV**, explored if WM and NVR could be trained respectively and elicit transfer effects to the other function, and whether training them together would result in benefits exceeding those expected. WM training increased WM capacity and NVR training improved fluid intelligence as well as a measure of WM. Training both functions improved both domains, but only at the expected level. **Study V** investigated the link between playing a musical instrument and cognitive benefits in a longitudinal design on individuals aged 6 to 25. Results showed that music practicing individuals showed a steeper development of visuospatial WM and NVR ability, and that this development was associated either with the type of instrument practiced (for NVR) or the number of hours per week they practiced (for WM).

These results illustrate that even though relations between cognitive functions are established, training or development of one does not automatically generalize to the others. Task requirements and appropriate load may be key differentiators between successful and non-successful interventions. Overall, this thesis presents evidence of early susceptibility to cognitive interventions and illustrates the complexity in the interrelations between higher order cognitive functions.

LIST OF PUBLICATIONS

I. McNab, F., Leroux, G., Strand, F., Thorell, L.B., **Bergman**, S., & Klingberg, T. Common and unique components of inhibition and working memory: an fMRI, within-subjects investigation (2008) *Neuropsychologia*, 46(11), 2668-2682.

II. Thorell, L.B., Lindqvist, S., **Bergman Nutley, S.**, Bohlin, G. & Klingberg, T. Training and transfer effects of executive functions in preschool children (2009) *Dev Sci*, 12(1), 106-113.

III. **Bergman Nutley, S.,** Söderqvist, S., Bryde, S., Humphreys, K., & Klingberg, T. Measuring working memory capacity with greater precision in the lower capacity ranges. (2010) *Dev Neuropsychol*. 35(1), 81-95.

IV. **Bergman Nutley, S.**, Söderqvist, S, Bryde, S., Thorell, L.B., Humphreys, K. & Klingberg, T. Gains in fluid intelligence after non-verbal reasoning training in 4-year-old children - a controlled, randomized study. (2011) *Dev Sci*, 14(3). DOI: 10.1111/j.1467-7687.2010.01022.x

V. **Bergman Nutley, S.** Klingberg, T. Music practice affects development of visuospatial working memory and non-verbal reasoning *Manuscript*

CONTENTS

LIST OF ABBREVIATIONS

EFs	Executive Functions
WM	Working Memory
WMC	Working Memory Capacity
IFs	Inhibitory Functions
NVR	Non-Verbal Reasoning
LTM	Long-Term Memory
ADHD	Attention Deficit Hyperactivity Disorder
Gf	Fluid Intelligence
Gc	Crystallized Intelligence
fMRI	Functional Magnetic Resonance Imaging
PFC	Prefrontal Cortex
DTI	Diffusion Tensor Imaging
TMS	Transcranial Magnetic Stimulation
Raven’s CPM	Raven’s Colored Progressive Matrices
Raven’s SPM	Raven’s Standard Progressive Matrices
Raven’s APM	Raven’s Advanced Progressive Matrices
IRT	Item Response Theory
RP	Repeated Pattern
SO	Sequential Order
CL	Classification

1 INTRODUCTION

The set of abilities that we use every day to think, function and interact in our social environment mature during childhood. These abilities are called higher order cognitive functions and are used every time we consciously focus on a task, remember what to do next, think of complicated matters or inhibit our inappropriate impulses. Their level of sophistication is what separates us from other animals and govern the way we think and ultimately act. In this thesis, some of these functions have been studied during typical development (Study III and V), and in adults with brain imaging techniques (Study I) and trained in preschoolers (Study II and IV). As these functions are imperative to complex thought processes, deficits in them are commonly associated with learning difficulties and inattention. It is therefore of great importance that we learn more about the mechanisms behind these functions, what their limitations are and if they are malleable. This thesis focuses on the interrelation between these functions, more specifically, whether they can be trained, whether training of one function will transfer to the other functions and whether they are dependent on the same neural resources.

1.1 EXECUTIVE FUNCTIONS

The set of abilities that enable complex cognitive processes are collectively called executive functions (EFs). This is a broad theoretical term that refers to deliberate control of thought, emotion, and ultimately action (i.e. goal-directed behavior) (Welsh & Pennington, 1988). Most definitions include working memory, inhibitory functions and flexibility/set shifting as part of the construct. They are key to higher order cognitive abilities such as logical thought processes, for instance non-verbal reasoning. Higher order abilities encompass all information processing in which monitoring and control play fundamental roles (Necka & Orzechowski, 2005).

EFs are involved only in novel or complex activities, such as inhibiting behavior, monitoring performance or formulating plans and strategies. In contrast, simple or routine task demands have been thought to be performed instinctively and hence without the involvement of EFs (Shallice & Burgess, 1990). However, this type of classification does not sufficiently accommodate the natural differences between individuals with regard to how simple, routine or novel and complex task demands are experienced to be (e.g. (Stuss & Alexander, 2000). This is of particular relevance when considering developmental differences between children and adults, as most tasks will be novel and complex for young children, thus requiring EFs to a larger extent.

EFs have been extensively studied for decades yet there is still no agreed upon definition. Most research points to a multifaceted divide into a handful of core functions. One influential theory stems from factor analytical variance and suggests subdivision of three main components that both share variance and contribute unique variance to the construct of EF; namely updating (of information in working memory), inhibition (of inappropriate responses) and shifting (switching between task conditions) (Miyake et al., 2000). The basis of the commonality was interpreted as an executive attention system (see also (Engle & Kane, 2004). These factors have since, in large, been replicated in developmental samples (Huizinga, Dolan, & van der Molen, 2006; Lehto, Juujarvi, Kooistra, & Pulkkinen, 2003). However, there seems to be a larger separation of the abilities during development, seen as differential developmental paths (Brocki & Bohlin, 2004; Carlson, 2005; Davidson, Amso, Anderson, & Diamond, 2006; Diamond, Kirkham, & Amso, 2002), with increased integration between functions from the age of 3 (Garon, Bryson, & Smith, 2008).

Executive processes are imperative to human behavior and have been shown to be mainly localized in the prefrontal cortex (PFC) of the brain (Duncan & Owen, 2000) but also depend on posterior and subcortical brain regions (Carpenter, Just, & Reichle, 2000). The PFC is extensively connected to virtually all other brain regions including the brain stem, occipital, temporal and parietal lobes as well as limbic and subcortical regions (Fuster, 1993). It is also among the last cortical regions to reach structural maturity (Gogtay et al., 2004; Shaw et al., 2008). The abilities constituting EFs work closely and complexly together and are difficult to study in isolation. That is one of the reasons why this system is still relatively poorly understood.

The work included in this thesis will focus on two of the three EFs described above as updating and inhibition, as well as the higher order function of non-verbal reasoning. Updating refers to the constant refreshing of material kept in working memory and will not be addressed further per se in this thesis. Instead focus lies on the work space in which for instance updating occurs: working memory. Inhibition will be addressed in terms of both interference control (preventing irrelevant information from entering working memory) and response inhibition (preventing inappropriate responses). Non-verbal reasoning refers to logical induction of relations between visuospatial materials.

1.1.1 Working memory

Working memory (WM) is the ability to temporarily keep a limited amount of information in an active state and either manipulate it (Baddeley, 1992), or according to alternative definitions, inhibit distractions from entering the active state (Kane & Engle, 2000). The scope of the temporal duration is in the proximity of 20 seconds (Goldman-Rakic, 1996). WM has a limited capacity which has been correlated with both general intelligence (Conway, Kane, & Engle, 2003; Engle, Tuholski, Laughlin, & Conway, 1999; Kane et al., 2004; Kyllonen & Christal, 1990), academic performance (Bull, Espy, & Wiebe, 2008; Gathercole, Pickering, Knight, & Stegmann, 2004), and is one of the core impairments in attention deficit hyperactivity disorder (ADHD) (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Baddeley and Hitch (1974) made a theoretical distinction between different components in WM. They separated different types of information into two storage components based on modality, the visuospatial sketchpad and the phonological loop. The visuospatial sketchpad was described as a mental blackboard temporarily holding visuospatial representations in the mental work space. For instance, information would be temporarily held there during visualization of a route from a map. The phonological loop theoretically supported the retention of verbal information where one of the more or less automated strategies to memorize information take place, namely rehearsal. This would be the work space we use when we try and remember a phone number while dialing or which steps to perform next while following a recipe.

The third component of the WM model consisted of the central executive which was a supervisory control system that managed the information in the two slave systems. The original WM model was revised by Baddeley in 2000, to include an additional component, the episodic buffer, which was proposed to hold a multimodal role integrating information between long term memory and WM. Since then, the central executive component of the model has been attributed with additional mechanisms including temporarily activating of long term memory (Baddeley, 1998), coordination of multiple tasks (Baddeley & DellaSala, 1996) and the capacity to attend and inhibit in a selective manner through switching processes (Baddeley, Emslie, Kolodny, & Duncan, 1998). This theoretical model has been extensively studied and even though the exact nature of the central executive (including the episodic buffer) remains unclear, the model still dominates the way WM is generally described.

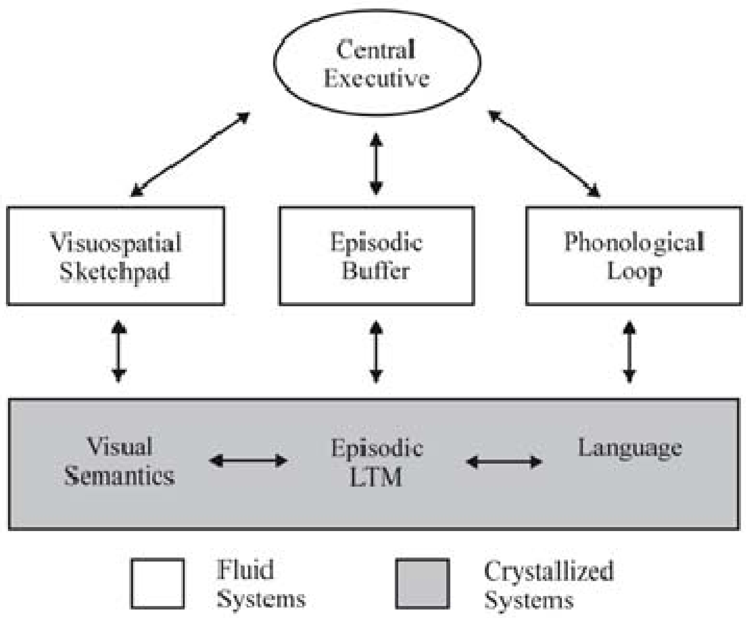


Figure 1. A schematic of the revised theoretical multi-component WM model revised by Baddeley in 2000. The visuospatial sketchpad deals with information that is visuospatial in nature, e.g. when trying to remember what to buy at the grocery store, you might visualize your fridge and then remember that the top shelf, where you normally keep the vegetables, was empty. If you made an inventory before leaving for the store, you might have decided that you didn't need to write a list but just make a memory list, which you will most likely rehearse in your phonological loop on your way to the store. At the store, you will most likely activate that memory list, which is now hopefully stored in your long term memory (LTM), through the episodic buffer and again recall it in the phonological loop. The central executive will be involved in retaining the list while deciding what the best route through the store is based on the items on the list. The "fluid systems" (in white) refer to processes dealing with transient information of varying nature whereas the "crystallized systems" (in gray) deal with semantic, learned information held in LTM.

1.1.1.1 Measuring WM

WM is commonly measured with tasks consisting of a memory component and distracting component requiring some additional processing of the remembered information. A typical task requires the subject to remember a number of stimuli and to repeat them in a specific order. In the verbal domain one might be presented with a list of digits to repeat in backwards order. In the visuospatial domain, one might view a number of sequentially presented stimuli to repeat in the correct order. These types of tasks are called span tasks and imply adding one more piece of information to be remembered at each level. The task generally ends when the subject fails to remember a sequence after a predetermined number of trials on the same level. The number of correctly recalled pieces of information constitutes ones' WM capacity. The degree of processing differs between tasks and ones that do not require manipulation of the information (storage only) to be remembered are generally referred to as simple span (or short-term memory, STM) tasks, whereas tasks requiring more processing (e.g. repeating digits in backwards order) are referred to as complex span tasks. This distinction will be discussed further in section 1.1.1.3.

1.1.1.2 Domain general/specific aspects of WM

The original WM model suggested that the central executive would be a domain general processing component common to both slave systems, which in turn would hold domain specific storage components (Baddeley, 1992). An alternative account was presented by Shah and Miyake (1996) who suggested that the WM system consists of two separate domain specific resource pools (verbal and visuospatial) that have independent capabilities of maintaining and manipulating the information. However, studies comparing STM and WM performance in both domains suggest a domain general processing component and domain specific storage components (Alloway, Gathercole, & Pickering, 2006; Bayliss, Jarrold, Baddeley, & Gunn, 2005; Bayliss, Jarrold, Gunn, & Baddeley, 2003), thus supporting the Baddeley & Hitch model. Further support for the domain general/specific components of WM come from neuroimaging studies where domain specific activation has been reported in superior temporal gyrus for an auditory task and in the occipital pole for a visual task, with domain general areas common for both tasks found for instance in the dorsolateral PFC (Klingberg, 1998). The brain areas known to be part of a core WM network include ventromedial and dorsolateral PFC and parietal cortex (Chein, Moore, & Conway, 2011; Curtis & D'Esposito, 2003; Klingberg, Kawashima, & Roland, 1996; see Linden, 2007 for a meta-analysis). The dorsolateral PFC activates specifically at higher loads (Rypma & D'Esposito, 1999) and is more active in individuals with high WM capacity (Edin et al., 2009; Linden et al., 2003) and the parietal has shown load sensitivity indicating for instance storage activity (Todd & Marois, 2005), or maintenance or shifting of attention among items held in WM (Berryhill, Chein, & Olson, 2011). These domain general areas have been proposed to represent attention processes.

1.1.1.3 Storage versus processing and relation to higher order abilities

Some studies suggest that the processing in WM is what drives the link with reasoning ability (Ackerman, Beier, & Boyle, 2005; A. R. A. Conway, Cowan, Bunting, Therriault, & Minkoff, 2002; de Abreu, Conway, & Gathercole, 2010; Engle, Tuholski, Laughlin, & Conway, 1999) whereas others find an equal share of explained variance between storage and storage + processing tasks (Colom, Shih, Flores-Mendoza, & Quiroga, 2006; Unsworth & Engle, 2007). This is subject to an ongoing debate in the research community. Also in the developing populations results show a mixed pattern between more unified and diverse relations between short term memory and WM. While some studies in children (aged 6-13) have shown that both verbal and visuospatial storage and executive processes respectively explain variance in reasoning independently (Bayliss, et al., 2005; Tillman, Nyberg, & Bohlin, 2008), others have found only executive processes to do so (in 5-9-year-olds) (de Abreu, et al., 2010). Possible explanations to these discrepancies include differences in the specific task requirements studied, scoring methods and ages studied. It may imply that the relation between domain specific and domain general components of WM differ throughout development. This was found in 4- to 6-year-olds who showed a closer relation between the visuospatial storage component and the processing component than older children (Alloway, et al., 2006).

1.1.1.4 Verbal versus Visuospatial and relation to higher order abilities

The domain specific storage systems have been reported to have different associations with academic profiles. Verbal WM has primarily been associated with attainment in English whereas visuospatial WM has been associated with English, mathematics and science attainment (St Clair-Thompson & Gathercole, 2006). The two slave systems also load differently on measures of general intelligence where the visuospatial system shows higher correlations with intelligence than the verbal construct (Kane, et al., 2004).

1.1.1.5 Relevance of studying WM

As previously mentioned, WM capacity (WMC) is correlated with reading, arithmetic performance (St Clair-Thompson & Gathercole, 2006), and more basic prerequisites of learning, such as following instructions (Engle, Carullo, & Collins, 1991; Gathercole, 2008) and is thus a determinant for academic achievement. Individuals with impaired WM will also be more easily distracted (Conway, Cowan, & Bunting, 2001) and report more mind wandering than individuals with high WMC (Kane et al., 2007). One of the possible mechanisms behind this is the ability to filter efficiently and it has been shown that low WMC individuals unnecessarily store irrelevant information to larger extent than individuals with high WMC (McNab & Klingberg, 2008; Vogel, McCollough, & Machizawa, 2005). Consequently, it is not surprising that impaired WM is one of the main problems in children with learning difficulties (Alloway, 2009; McLean & Hitch, 1999). It is also commonly impaired in many clinical populations including individuals with traumatic brain injury (McDowell, Whyte, & DEsposito, 1997), specific language impairments (Archibald & Gathercole, 2006), schizophrenia (Pukrop et al., 2003), and in individuals born preterm (Luciana, Lindeke, Georgieff, Mills, & Nelson, 1999).

WM deficit is also one of the central findings in ADHD (Dowson et al., 2004; Kempton et al., 1999; Martinussen, et al., 2005; Westerberg, Hirvikoski, Forssberg, & Klingberg, 2004; Willcutt, et al., 2005), where inattention is the behavioral consequence. Children with ADHD have difficulties remembering and consequently following lengthy instructions and easily lose focus because of it. Strategies to alleviate the strains on WM are typically employed by educators to children with ADHD. These strategies include segmenting instructions in to several parts, increasing meaningfulness and familiarity of material, restructuring complex tasks and using memory aids (Gathercole, 2008). In a meta-analysis by Martinussen (2005) it was reported that impairments in the visuospatial domain were more severe than in the verbal domain compared with controls. Given the wide range of clinical populations experiencing WM deficits, it is of great importance to learn more about the biological underpinnings, early identification of deficits, possible WM alleviation as well as WM remediation strategies.

1.1.2 Inhibitory functions

Inhibitory functions (IF) are also parts of the term EFs and generally refer to processes of preventing impulses to take action and/or preventing distracting information from interfering. IFs are fundamental to our daily repertoire of human behavior and their sophistication levels differentiate us from the animals. Humans typically develop superior control over instinctive, but sometimes inappropriate, responses to stimuli. The nomenclature regarding IFs is less agreed upon than for WM but the complexity of IFs do call for a subdivision of some kind. Two of the different subtypes that this thesis does not deal with are; delay aversion, which is the ability to delay gratification, and shifting, which is the ability to quickly adapt to rule switching by inhibiting formerly learned rules. These types of IFs will not be discussed further in the thesis but should be mentioned as other important variants. The theory that provides the framework for the research on inhibition included in this thesis was proposed by Barkley (1997). He used the term “behavioral inhibition” and suggested that it be viewed as separate from EFs and instead prerequisite processes for successful executive functioning. He divided them into (1) inhibiting an initial pre-potent response, (2) inhibiting an ongoing response and (3) inhibiting interference from irrelevant information. He suggests that this system exerts direct control over motoric action and merely sets the occasion for when EFs can perform. This model was based on different aspects identified as difficulties in children with ADHD.

1.1.2.1 Measuring IFs

IFs are generally measured with tasks requiring either a withheld motor response or a different response than a pre-potent one. The former is generally called response inhibition and will subsequently refer to tests assessing (1) and (2) from the Barkley model (see above). The latter includes tests that assess distractibility or interference control. A test of response inhibition commonly consists of a go-signal, requiring the subject to make speeded motor responses and more seldom, no-go-signals, requiring the subject to withhold the motor response, which has become pre-potent throughout the performance of the task. Failure to withhold an inappropriate response is categorized as a commission error whereas failure to appropriately respond (on go-trials) is termed an omission error.

A test of interference control entails inhibition of irrelevant stimuli, and consequently making a different response than the instinctive one. For example, in the Eriksen Flanker task (1979), a subject would view a set of horizontal arrows which all point in the same direction and be asked to respond in accordance with the central arrow's direction. When the central arrow points in the opposite direction of the surrounding ones, the subject must resist interference from the surrounding ones in order to make a correct response. This is typically accompanied by longer reaction times and decreased accuracy and the difference in reaction time between the two conditions acts as the quantifiable measure of interference.

Evidence from neuroimaging, neuropsychology and transcranial magnetic stimulation (TMS) suggests that response inhibition relies on inferior frontal activation, particularly in the right hemisphere (Garavan, Ross, & Stein, 1999; see Aron, 2007 and Chambers, Garavan, & Bellgrove, 2009 for recent reviews). Inferior frontal gyrus has been identified as a central area for response inhibition (Aron, Robbins, & Poldrack, 2004; Booth et al., 2003; Rubia et al., 2001) and has been associated with longer reaction times on incongruent trials in a Flanker task (Hazeltine, Poldrack, & Gabrieli, 2000). Other areas reported common to response inhibition and interference control are dorsolateral PFC, anterior cingulate and dorsal premotor cortex (Chambers, et al., 2009).

1.1.2.2 IF and relation to higher order abilities

IFs are fundamental to staying focused on any given task in order to achieve the goal and are as such naturally related to higher order cognitive abilities. As previously mentioned it has been argued that the processing component of WM would be stronger related to higher-order abilities (Engle, et al., 1999; Kane, et al., 2004). This component relies on inhibiting interfering information from entering WM and is thus an integral part of this relation. Further support for the close link between WM and interference control lies in the previously mentioned coexistence of poor WM and tendency to distraction (Conway, et al., 2001). In fact, some theories propose that interference control is an innate aspect of WM (Engle & Kane, 2004). There is evidence that the relationship between these abilities may change throughout development which will be discussed in a later section. As IFs do not appear to be unitary and it is thus likely that the subcomponents are differently related to higher order abilities. For instance, IFs have been argued to be neglected dimensions of intelligence, where interference control in particular has been emphasized as essential for complex cognitive functioning (Dempster, 1991). The link between response inhibition and intelligence is less clear but low intelligence scores have been correlated to increased number of commission errors made in a Go/No-go task (Horn, Dolan, Elliott, Deakin, & Woodruff, 2003). IFs are also predictive of academic performance, specifically in math (Bull & Scerif, 2001) and reading comprehension skills (Borella, Carretti, & Pelegrina, 2010). IFs are integral parts of self-discipline as it involves resisting distraction and inhibition of perhaps more appealing activities. Self-reported self-discipline has also been associated with academic performance (Duckworth & Seligman, 2005).

1.1.2.3 Relevance of studying IFs

Besides the importance of IFs to complex thought processes, IFs are commonly impaired in a number of developmental disorders. Symptoms of hyperactivity and impulsivity are central to diagnosis of ADHD. Impulsivity can be described as the behavioural consequence of deficits in the IFs (APA, 1994). Failure to inhibit inappropriate responses will lead to stimulus driven behaviour, where the interaction level with the environment will be high. This occurs in children as developmental stage where interrupting conversation, running in to the street without looking and failing to resist temptations are conceived as natural but immature behaviour. When this type of behaviour persists and is no longer age appropriate it is commonly linked with a diagnosis. Besides in ADHD (Hervey, Epstein, & Curry, 2004; Willcutt, et al., 2005), impaired IFs have been reported in Tourette’s syndrome and high functioning autism (Verte, Geurts, Roeyers, Oosterlaan, & Sergeant, 2006) as well as in borderline personality disorder (Nigg, Silk, Stavro, & Miller, 2005) and in typical aging (Kramer, Humphrey, Larish, Logan, & Strayer, 1994). Detection of impaired IFs is commonly instigated by behavioural difficulties but can perhaps show different neuropsychological profiles in the effected abilities. This is important in order to find appropriate strategies for interleaving the difficulties as well as understanding in which domains specifically the problems are focused (response inhibition versus interference control for example).

1.1.3 Non-verbal reasoning

Non-verbal reasoning (NVR) is the process in which visuospatial stimuli are analysed and compared in order to discover the logical rules that govern the relation between them, and applying these rules when making a response (a description similar to the definition of “inductive reasoning” (Carroll, 1989) but exclusively visuospatial in nature). It is the underlying measurable function to the latent term fluid intelligence. To clarify this distinction a brief background in intelligence research is warranted. The formal study of complex cognitive functioning has been pursued since the end of the 19th century. One of the founding fathers of the psychometric approach was Alfred Binet, who in order to objectively measure and identify individuals who needed additional educational support, created a set of tests that filled this function. These types of tests were later found to correlate with each other and the common factor between them was defined by Charles Spearman (1927) as general intelligence or *g* (corresponding to the composite score of IQ which is the age normed individual score from several tests). In order to study developmental differences between individuals, a further distinction between tests within these batteries was proposed by Cattell (1963) into fluid intelligence (*Gf*) and crystallized intelligence (*Gc*). *Gf* was described as the common factor between tests requiring discrimination and perception of relations, whereas *Gc* depended on learned (through *Gf*) facts and rely on experience (see Figure

1 for a parallel division in Baddeley's WM model). These terms are statistical definitions as they are derived from common variance analyses and will therefore only be used to refer to constructs undergone similar analyses. Tests constituting the term *Gf* generally assess NVR.

1.1.3.1 Measuring NVR

Tests measuring NVR consist of visuospatial figures creating an incomplete task to either sort by specific features of the stimuli, identify and continue patterns or complete sequences. They may differ in complexity requiring as little as one dimension of rule detection (e.g. colour) or several dimensions (e.g. colour, size of stimuli, position of stimuli in relation to other ones etc.). A common NVR test is Raven's Progressive Matrices. Each item consists of an incomplete figure and the respondent has to select one out of 6 or 8 options to complete the figure. There are different versions of the test suitable for different ages and capacities, starting with Raven's Coloured Progressive Matrices (CPM) proceeding to Raven's Standard Progressive Matrices (SPM) and finally, Raven's Advanced Progressive Matrices (APM). Other NVR tests include; classification tasks, in which one is required to detect the rule, and sort stimuli based on it (e.g. shape); sequential ordering tasks, in which one should correctly continue the partially displayed sequence; and repeated pattern tasks which require the identification of a pattern and the continuation of it. The common components should be to identify relations, deduce rules and apply them to solve the task.

Neuroimaging studies indicate activation of rostrolateral PFC during performance on Raven's SPM tasks (Christoff et al., 2001). In addition, parietal cortex has been associated with greater activation during performance on relational reasoning in high IQ individuals compared to average scoring IQ individuals (Lee et al., 2006). This fits well with the finding that adults show greater activity in the inferior parietal compared with children during performance on relational reasoning tasks (Crone et al., 2009). Furthermore, performance on Raven's APM predicted activity in the lateral PFC and parietal on WM trials with high load on interference (Gray, Chabris, & Braver, 2003). Overlaps between WM and reasoning tasks have been reported in bilateral middle occipital gyri, the posterior cingulate and the medial and superior frontal gyri (Ruff, Knauff, Fangmeier, & Spreer, 2003).

1.1.3.2 Relevance of studying NVR

As mentioned in the definition of *Gc*, it relies on the construct of *Gf* to learn factual information. The *Gf* construct is therefore the core prerequisite for learning and understanding and is at the very top of the hierarchy in cognitive complexity. It is sometimes referred to as a higher order cognitive ability because it relies on subordinate systems, such as WM and IF in order to function. As described in previous sections, the importance of WM to NVR is indisputable as the identification and induction of rules require temporary memory storage while being processed; hence the inseparability of the two functions. It is my understanding that it is not possible to construct a NVR test that does not require WM, and to some degree the same is true for interference control. Therefore, the relevance of studying NVR are partly encompassed by the previously mentioned reasons to study WM and IFs. Unsurprisingly, studies have shown a high correlation between IQ and scholastic performance (Luo, Thompson, & Detterman, 2003; Lynn, Meisenberg, Mikk, & Williams, 2007).

1.1.4 Role of attention

Attention is perhaps the most intricate function to define and study, because of its' near constant presence in the conscious mind. Just as it is impossible to study NVR without studying WM, it is just as impossible to study WM or interference control without studying attention. In fact, a shared feature of different EF models appoints the commonalities between different EFs to an executive attentional component. For example, in Miyake's model (2000) the shared variance between the core EFs consisting of shifting, updating and inhibition was discussed as "controlled attention". Likewise in a model proposed by Cowan (1988) the information held in temporary storage is held there as long as it is at the center of focused attention and will decay or suffer from interference only when attention wonders (Cowan, 2010). Other differentiations between attention types are: bottom-up versus top-down. This implies stimuli driven, reactive attention for the former and conscious, controlled, goal oriented attention for the latter. Posner (1990) has differentiated the term attention into: orienting (stimulus driven/bottom up), detecting signal for conscious processing (executive attention/top-down) and maintaining an alert state (sustained attention) (Posner & Petersen, 1990). These different types of attention are uncorrelated with each other (Fan, McCandliss, Sommer, Raz, & Posner, 2002). In this theory, interference control is a process encompassed in the attention system and not in the IFs or WM. This type of terminology confusion makes the field of EFs particularly difficult to overview as different researchers use different terms to refer to the same function. Furthermore, task demands differ and influence the results and interpretation of them substantially (as discussed for attention in the visual STM and WM systems by Astle & Scerif, 2010). For instance maintaining an alert state is essential for any type of prolonged test of cognitive function and is thereby often assessed whether it is intended or not, however only rarely discussed.

The term "attention" is perhaps better used at the behavioral level as everyone knows what is referred to when told to "pay attention". Exactly which elements that enable that function and what their nomenclature should be is still unclear. As most other commonly disputable issues, it all comes down to definitions. Most researchers would agree that attention is a much too vague term to contribute any real understanding of cognitive functions and their interrelations. Since the research field still has not reached consensus regarding the definition of attention, I will refrain from attempting one, but merely acknowledge the fact that attentional processes are very present in all three EFs studied here. To which extend and the relevance thereof will only briefly be discussed.

1.2 DEVELOPMENT OF WM, IF AND NVR ABILITIES

It is self-evident that there is a gradual development of the functions that allow planned, deliberate and flexible behaviour. While the focus of this thesis lies in slightly older individuals, a brief background in the development of EFs during infancy will be provided. Historically, study of the development of EFs have much of its origin in observation of natural maturation. Piaget observed his three infants sensorimotor development and noted behavioural milestones in the understanding and interaction with the environment. He noticed that infants younger than 7 months failed to accurately retrieve a hidden object after a short delay period, if the object’s location was changed from one where it was previously and successfully retrieved. Infants of this age often make a particular error in reaching for the location in which the object was hidden in the previous trial. This characteristic error, called “A not B” was interpreted by Piaget (1954) as evidence of failure to understand that objects remain when moved from view. This may have been a drastic conclusion and extensive research has suggested alternative explanations to this behaviour.

A (by Piaget) overlooked component in this task was the memory aspect, which was manipulated by altering the delay period after which the child was allowed to search for the object. Diamond (1985) found that the delay necessary to produce the A not B error increased with around 2 seconds per month across the age span of interest and at 12 months, errors only occurred with delays of 10 seconds or more. Furthermore, results suggest that besides memory, inhibiting the pre-potent response (in this case search at A) is key to successful A not B performance (Diamond, Cruttenden, & Neiderman, 1994). This “simple” task illustrates that EFs begin development already in infancy and illustrate the intricate relation between them. Despite this intricacy, evidence of differential rates of development and hence distinctly separable functions has reinforced the notion of EFs as a multicomponent construct.

An obvious problem when reviewing developmental findings are comparisons between different ages. Studies including specific and narrow age ranges may find different interrelations between functions than other ones. Another problematic issue with developmental studies is adjusting task difficulty to age appropriate levels. It is a great challenge to create tests that tap each of the abilities at the same proportionate difficulty across different ages. This will be addressed for WM specifically in Study III but extends to all psychometric testing of abilities. The motivation behind Study III arose from the observation (in study II and from previous literature) that the variability on WM Span tasks in the lower capacity ranges was quite poor. Almost all 4-5-year-old children in Study II remembered 3 or 4 dots in a visuospatial Grid task and this is not enough variability to effectively discriminate between abilities. Even though previous research has identified factors determining the difficulty of remembering a specific visuospatial pattern (Busch, Farrell, Lisdahl-Medina, & Krikorian, 2005; Kemps, 2001; Orsini, Pasquadibisceglie, Picone, & Tortora, 2001), no attempts aimed at utilizing this information in creating more precise measurements (e.g. by creating sub-levels) have been reported. As EFs can predict school readiness, math performance and consequentially also academic difficulties, it is important to have reliable and precise measures of EFs throughout development. The development of each of the three functions of WM, IFs and NVR will be discussed separately. But first, a few words on the development of the commonalities between EFs.

The model on the common components of EFs presented by Miyake and colleagues (2000) based on adults has since been extended to child populations (for a review, see (Best & Miller, 2010). The main findings suggest that the three EF components inhibition, WM and shifting can be detected in preschoolers (Garon, et al., 2008), children aged 8-13 (Lehto, et al., 2003) and possibly also up to the age of 21 (inhibition tasks did not load on one single factor in a study on 7-21-year-olds, (Huizinga, Dolan, & van der Molen, 2006b). Maturation of the EFs have been discussed as partly due to development of executive attentional networks which has been found to go through rapid development during preschool years (Rothbart, Ellis, Rueda, & Posner, 2003). However, EFs develop at different rates and consequentially; the interrelation between the functions may change with development (Davidson, et al., 2006). These differential relations across development may imply that training of the separate functions at different developmental stages may elicit differences in transfer effects.

1.2.1 Development of WM

As mentioned, the ability to form mental representations of objects no longer in plain sight during a delay period shows existence and development already in the first year of life (Diamond, 1985). A large study assessing the components of the Baddeley and Hitch WM model in children aged 4 to 15 confirmed the existence of the phonological look, visuospatial sketchpad and the central executive across development (Gathercole, Pickering, Ambridge, & Wearing, 2004). Furthermore, all components showed a steady linear development and confirmed the relative independence of the two slave systems. Furthermore, the relation between the visuospatial storage and the domain general processing component (central executive) seem more closely linked in 4 to 6-year-olds (Alloway, et al., 2006), suggesting that visuospatial storage requires central executive support to a larger extent than verbal storage in this age group.

The specific functions explaining increased WM capacity are still not clear cut although theories include increased efficiency/speed in processing (Demetriou, et al. 2002; Fry & Hale, 2000) and more efficient filtering of irrelevant information or controlled attention (Astle & Scerif, 2010; Cowan, 2010; McNab & Klingberg, 2008; Vogel, et al., 2005). A recent study on 6- to 24-year-olds found that processing speed accounted for 73% of the variance in the increased WM performance with development, but that there was still an effect of age after controlling for processing speed (McAuley & White, 2011). This indicates that processing speed is one of the key underlying factors, but not the only one, to WM development.

Neurophysiological evidence suggests that children only weakly recruit the core WM regions of dorsolateral PFC and parietal regions, and instead rely primarily on ventromedial regions (Scherf, Sweeney, & Luna, 2006). With development, recruitment of prefrontal and parietal areas increase (Klingberg, 2006; Klingberg, Forssberg, & Westerberg, 2002a) along with specialization and integration with performance enhancing regions in adulthood (Bunge & Wright, 2007; Scherf, et al., 2006). Furthermore, evidence from a study using Diffusion Tensor Imagine (DTI) has shown a superior fronto-parietal region in which maturation of white matter was correlated with the development of WM (Nagy, Westerberg, & Klingberg, 2004). A possible explanation to these findings on the cellular level is increased synaptic connectivity between cells coding for similar stimuli (Edin, Macoveanu, Olesen, Tegner, & Klingberg, 2007).

1.2.2 Development of IFs

While rudimentary forms of inhibition are seen already during the first year (Diamond, 1990), they do not become fully matured until late adolescence/early adulthood (Diamond, 2002; McAuley & White, 2011). Studies using more complex inhibition tasks have provided information on the relative difficulty between IF and WM during development and shown that IFs generally develop at a slower rate than WM does. This was illustrated in a large study by Davidson and colleagues (Davidson, et al., 2006) using a task including both inhibition and WM taxing components assessing children aged 4 through 13. They found that the youngest children could hold information in mind, inhibit a dominant response, and combine those conditions when the inhibition required was steady-state and the rules remained constant. However, when the task required cognitive flexibility, switching between inhibition and no-inhibition trials, the children were more affected than the adults, with 13-year-olds still not performing at adult levels. This indicates differential strengths in the interrelations between WM and IF across development (Davidson, et al., 2006) and further support for integration of the two functions with age has been reported since (Roncadin, Pascual-Leone, Rich, & Dennis, 2007). In a study by Carlson and colleagues (2005) children aged 3 and 4 were tested with the “Less is more” task requiring them to point to a smaller reward in order to receive a larger one. There was significant performance improvement with age and additionally, improvement over trials for the 4-year olds, but not the 3-year-olds, indicating a learning effect for the older children. This suggests that significant changes take place in IF during the preschool ages.

One of the underlying factors explaining the development of IF has been shown to be processing speed. It was recently shown that developmental increases in processing speed explained 89% of the development of response inhibition and the age effect was no longer significant when processing speed was controlled for (McAuley & White, 2011).

1.2.3 Development of NVR

Given the close relation between WM and NVR (e.g. Engle, et al., 1999; Kyllonen & Christal, 1990) and the dependency of NVR on WM it is not surprising that their development is linked. In a recent study on 8-14-year olds a developmental cascade effect was observed where chronological age was accompanied by faster processing speed which influenced WM, which in turn influenced NVR ability (Nettelbeck & Burns, 2010). Similar results have been reported previously (Fry & Hale, 2000) as well as demonstrated in longitudinal studies (Demetriou, Christou, Spanoudis, & Platsidou, 2002). Regardless of the underlying force, the psychometric findings indicate that NVR increases rapidly in early and middle childhood, continuous to increase at a slower rate until early adolescence after which it reaches asymptote in mid-late adolescence (McArdle, Ferrer-Caja, Hamagami, & Woodcock, 2002).

1.3 COGNITIVE TRAINING

Cognitive training refers to processes that target cognitive abilities in order to increase their capacity. It has been attempted with many different approaches, including memorizing long sequences of numbers, learning strategies to solve problems and more alternative techniques, e.g. meditation. The term cognitive training will in this thesis only refer to repeated practice on tasks tapping specific functions. This type of training has been shown to produce larger transfer effects than for instance strategy training, perhaps due to training of underlying processes that might be shared with other cognitive functions (Morrison & Chein, 2011; St Clair-Thompson, Stevens, Hunt, & Bolder, 2010).

1.3.1 WM training

Traditionally, WM has been shown to be a relatively stable function that after developmentally reaching its full capacity, remains at approximately the same level throughout most of adulthood until it declines slightly with ageing (Craik, 1990). Consequently, it has also been assumed that WM capacity is fixed within an individual. Over the past decade it has, however, been well established in a rapidly growing body of research, that WM can be improved with training. This has been shown in children with ADHD (Holmes et al., 2009; Klingberg et al., 2005; Klingberg, Forssberg, & Westerberg, 2002b), WM deficits (Holmes, Gathercole, & Dunning, 2009), learning difficulties (Dahlin, 2010), low socioeconomic status (Mezzacappa & Buckner, 2010), healthy controls (Dahlin, Neely, Larsson, Backman, & Nyberg, 2008; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; McNab et al., 2009; Olesen, Westerberg, & Klingberg, 2004), healthy elderlies (Borella, Carretti, Riboldi, & De Beni, 2010) as well as in adults with acquired brain injury (Lundqvist, Grundstrom, Samuelsson, & Ronnberg, 2010; Westerberg et al., 2007, see Klingberg, 2010 for a review). This type of training involves intense practice over the duration of weeks on tasks tapping WM. Difficulty is adapted to each individual’s capacity with an adaptive algorithm adjusting progress in difficulty based on the performance on the previous trials. This has been shown to be essential for improvement in that training on low levels of WM trials does not lead to substantial improvement (Klingberg, et al., 2005; Klingberg, et al., 2002b). In fact this type of low level training has often been implemented as an active control condition, thus differing only in the proposed key ingredient (training at the capacity limit) compared to the principal condition (Beck, Hanson, Puffenberger, Benninger, & Benninger, 2010; Holmes, Gathercole, & Dunning, 2009; Klingberg, et al., 2005; Klingberg, et al., 2002b).

The effect of WM training has shown to increase performance on tasks measuring NVR (as tested with Raven’s SPM) (Jaeggi, et al., 2008; Klingberg, et al., 2005; Klingberg, et al., 2002b), IF (tested with Stroop) (Chein & Morrison, 2010; Klingberg, et al., 2005; Klingberg, et al., 2002b; Olesen, et al., 2004) and sustained attention (tested with Pased Auditory Serial Addition Test) (Westerberg, et al., 2007). Furthermore, training effects extend to behavioural improvements in symptoms of inattention (Beck, et al., 2010; Klingberg, et al., 2005; Mezzacappa & Buckner, 2010). Training effects have also been reported in reading comprehension (Chein & Morrison, 2010; Dahlin, 2010) as well as additional delayed effects in arithmetic evident 6 months following training (Holmes, Gathercole, & Dunning, 2009). This implies that the improvements seen in WM after training can alleviate and support academic achievement in both the reading and mathematics domains.

The biological underpinnings to the training effects have been studied (for a review see Klingberg 2010. The main findings after WM training show an increased activity in prefrontal, parietal cortices and caudate nucleus after training (Olesen, et al., 2004), increased structural connectivity in white matter in intra parietal sulcus possibly representing myelination (Takeuchi et al., 2010), and an altered density of dopamine D1 receptor, both in the prefrontal and parietal cortex (McNab, et al., 2009). These findings illustrate plasticity in this system resulting from repeated activation of the WM network.

1.3.2 Inhibition training and/or training of attention

Since there is some confusion on the field regarding the nomenclature on interference control as part of Ifs, WM or attention, a functional approach will be taken in reviewing the literature on this topic. One study trained a small group of children (n=7) with ADHD on a wide range of board games and computer tasks during 8 weeks (Kerns, Eso, & Thomson, 1999). The games that were used targeted sustained, selective (interference control), alternating and divided attention with modest effects seen on interference control (e.g. Stroop) and sustained attention (Underlining test), planning (Mazes) and a math test, compared to the control group.

A different and computerized intervention was tested on preschoolers (4- and 6-year-olds) who received 5 sessions of broadly defined attentional training (Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005). The results showed an improvement on measures of intelligence (K-BIT) in the 4-year-olds, but not for the 6-year-olds, and no improvements on interference control (tested with Flanker task) for either age group. A similar regime was employed for a group of children with ADHD receiving 8 weeks of attentional training (targeting the components proposed by Posner and Peterson 1990) or video game playing (Shalev, Tsal, & Mevorach, 2007). The active training condition significantly improved performance on passage copying, reading comprehension and behavioural ratings of inattention. Interference control has also been trained in healthy adults with significant improvements on reaction times on conflict resolution tasks (Persson & Reuter-Lorenz, 2008).

A different approach was used by Dowsett and Lively (2000) in that preschoolers (aged 3-5) with inhibition difficulties received 3 sessions of training either on a simple Go/No-go task or a flexibility/card sorting task as well as a switching task/discrimination learning task. The groups were compared to a control group and results showed significant improvements in response inhibition for both training groups with an additional advantage for the switching training group. There was also an effect of age indicating larger improvements for the older children.

Diamond and colleagues (2007) have shown improvements on tests of IFs for children having participated in a preschool program targeting EFs directly on the behavioural level. The intervention was implemented by the teachers in the preschools and results have been shown for 147 children undergone one or two years of EFs or control curriculum. The results showed that the children receiving EFs curriculum significantly outperformed the control children on simple IFs tests (response inhibition and a Flanker task) with even larger differences between groups seen on more complex switching tasks. Switching tasks pose both response inhibition and WM demands because the response mode is tied to different rules, which must be remembered throughout the test.

These findings collectively suggest that it is possible to train aspects of IFs, even though the effects on the interference control aspect of IF has been more commonly reported than the response inhibition domain.

1.3.3 NVR training

The theoretical assumptions underlying the definition of fluid reasoning was that of a fixed trait that was independent of experience and prior knowledge (Horn & Cattell, 1967). However, recent studies suggest that this may in fact not be true. Studies reporting improvements on NVR tests stem from different approaches (see Buschkuehl & Jaeggi, 2010 for a review). Initial training attempts have used strategy training where the subjects are taught how to address the NVR problems in a step by step manner, resulting in increases in NVR performance. This was first reported for older individuals (Plemons, Willis, & Baltes, 1978; Willis & Schaie, 1986) but has also been studied in children receiving classroom instructions on divergent thinking and creative problem solving (Hamers, de Koning, & Sijtsma, 1998; Herrnstein, Nickerson, de Sanchez, & Swets, 1986; Klauer & Willmes, 2002; Stankov, 1986). These studies have neither been randomized nor had active control groups, making conclusions on the effectiveness of the method uncertain. It has however been shown that it is possible to significantly increase performance, compared to controls, on Raven’s SPM/APM after only a few minutes of strategy training (Denney & Heidrich, 1990). This indicates that the way in which to successfully tackle a NVR task can be taught. However, other underlying factors, such as WM capacity, may limit performance even if you, in theory, know *how* to solve the problem. Furthermore, being told how to solve something or coming up with the solution on your own, may draw upon different cognitive skills, e.g. applying the rule versus inducing *and* applying the rule. On test performance, the outcome from the procedures may appear to be the same, even though the approaches to solve the problem may differ and lead to different skill development.

A recent study (published after Study IV was accepted) included 7-10-year-olds with low socioeconomic background, using a wide range of commercially available games to train either processing speed or NVR (Mackey, Hill, Stone, & Bunge, 2010). They did not include a traditional control group but expected only minimal transfer between the two training constructs and thus used the other group as a control condition. Results showed a trend toward an increase in NVR for the NVR training group compared with the processing speed training group. Furthermore, the NVR group showed a significant improvement on a WM test, the spatial span task.

Other targeted approaches to try and affect underlying functions of NVR, such as WM, have also generated increases on NVR tasks in children with ADHD (Klingberg, et al., 2005; Klingberg, et al., 2002b) and adults using either a single updating task (Jaeggi et al., 2010) or a dual updating task (Jaeggi, et al., 2008). As previously mentioned, findings from attention training resulted in increases in intelligence for the 4-year.olds but not for the 6-year-olds (Rueda, et al., 2005). Increases in NVR have also been reported after music lessons in children (Rauscher et al., 1997; Schellenberg, 2004) (see next section). Taken together, these findings point in the direction that NVR is perhaps not as fixed as previously assumed.

1.3.4 Training cognitive functions through music practice

Studies on cognitive training generally aim to improve functions needed for everyday activities, and not surprisingly it seems that certain everyday activities tapping cognitive functions may also train them in return. A field that has been relatively extensively studied is the effects of music practice on cognitive functioning. Professional musicians have been studied with neuroimaging techniques revealing music related brain increases in grey matter volume in both auditory discrimination areas (Gaser & Schlaug, 2003; Hyde et al., 2009), motor areas (Elbert, Pantev, Wienbruch, Rockstroh, & Taub, 1995; Hyde, et al., 2009) as well white matter volume in motor tracts (Bengtsson et al., 2005). More recently, associations between music practice and cognitive performance have been reported (Forgeard, Winner, Norton, & Schlaug, 2008; Ruthsatz, Detterman, Griscom, & Cirullo, 2008; Schellenberg, 2006). Specifically, higher performance has been reported in tasks requiring NVR (Bilhartz, Bruhn, & Olson, 1999; Costa-Giomi, 1999; Forgeard, et al., 2008; Hurwitz, Wolff, Bortnick, & Kokas, 1975; Schellenberg, 2006) and WM, both for the verbal (Bugos, Perlstein, McCrae, Brophy, & Bedenbaugh, 2007; George & Coch, 2011; Lee, Lu, & Ko, 2007; Schellenberg, 2006) and for the visuospatial domain (George & Coch, 2011; Lee, et al., 2007). Furthermore, a causal link from music practice to enhanced cognitive functioning has been demonstrated in a controlled, randomized study of 4-year-olds who received one school year of either: piano-, vocal-, drama- or no classes (Schellenberg, 2004). Children in the music groups showed increased IQ scores compared with the control groups, indicating that music lessons affected the development of cognitive functions. A similar study on preschoolers reported superior gains in a NVR task for a piano playing group compared with a singing and other control groups after 6-8 months of lessons (Rauscher, et al., 1997). The active ingredient affecting cognitive abilities can be discussed, and while some suggest that commonalities between solving spatial tasks and musical practice lie in the similar hierarchical organization of spatial and aural representations (Gromko & Poorman, 1998), others propose that the effect comes from multifaceted cognitive control demands including for example the decoding of musical notation (Schellenberg, 2006). This is plausible given the correlations between sight reading and IQ (r = 0.6) (Salis,

1978) and sight reading and WM (*r* = 0.3-0.4) (Meinz & Hambrick, 2010; Salis, 1978). Further support from neuroimaging studies suggest a partial overlap in the typically recruited WM and spatial brain areas in the parietal while reading musical notation (Bengtsson & Ullen, 2006; Nakada, Fujii, Suzuki, & Kwee, 1998; Schon, Anton, Roth, & Besson, 2002; Stewart et al., 2003).

2 AIMS

The general aim of this thesis was to investigate the interrelation between higher order cognitive functions in children and adults by using either: targeted training interventions, developmental designs or functional magnetic resonance imaging (fMRI). Specifically, we aimed to study; the relation between WM and IFs (**Study I and II**), the effects of targeted cognitive training of either: WM (**Study II** and **IV**), IFs (**Study II**), NVR, or both WM and NVR (**Study IV**) in preschoolers and finally, the effects of musical practice on WM and NVR (**Study V**).

Additional objectives for each study were to investigate:

Study I
- if there is overlapping activation in brain areas while performing inhibition tasks and WM tasks (as studied with fMRI)

Study II
- if it is possible to train WM in preschoolers
- if it possible to train IFs in preschoolers
- if training either WM or IF will lead to improvements in the other respectively

Study III
- if it is possible to create a more precise test for measuring visuospatial WM in the lower capacity ranges

Study IV
- if it is possible to improve Gf through training on NVR tests
- if training either WM or NVR will lead to improvements in the other respectively
- if training both WM and NVR will lead to synergistic effects

Study V
- if musical practice will lead to cognitive benefits in WM and NVR
- if musical practice will differ between instruments requiring dual-staff and single-staff score reading
- if the effects of musical practice are dose dependent

3 METHODS

3.1 PARTICIPANTS

In Study I, 14 right handed healthy volunteers participated after giving informed written consent. The data from 11 participants were included in the fMRI analysis (*M* = 24 years, *SD* = 4 years, range 22-34, 4 males).

Study II included 65 children born in 2001, aged 4 and 5 (*M* = 56, *SD* = 5.18) at the time of the study. Informed written consent was obtained from one caregiver of each of the participating children. All children at two preschools in Uppsala and two in Stockholm were asked to participate. One of the schools in Uppsala formed the active control group whereas one of the schools in Stockholm formed the passive control group. The participants at the remaining two schools were randomized, after matching them by gender and age, to train either IF or WM games.

Study III entailed Experiment 1 and Experiment 2 which both included 4- and 6-year-old children. The subjects were recruited from preschools in Stockholm and written informed consent was obtained from one parent of all participating individuals. Twenty-two children aged 4 (mean age: 53 months, *SD* = 3.9, 12 girls) and 15 aged 6 (mean age: 76 months, *SD* = 3.2, 9 girls) participated in Experiment 1, and 27 children aged 4 (mean age: 50 months, *SD* = 2.1, 9 girls) and 33 children aged 6-7 (mean age: 83 months, 13 girls) participated in Experiment 2.

In Study IV, the participants were recruited through preschools, flyers, the lab webpage and advertisements in the local papers. We included 112 children with the age range of 4 to 4.5 years (mean age 51 months, *SD* = 3.0, 44 girls). Informed written consent was obtained from one of each child's caregiver.

Study V includes subjects participating in the Brain Child study, which is a large longitudinal investigation of development of memory functions and their relation to academic achievement, life style factors and biological measures. Subjects were randomly selected from the Swedish population registry in the town of Nynäshamn and were between the ages of 6 and 25 (more specifically 6, 8, 10, 12, 14, 16, 18, 20 and 25 years old) at the first testing point (n=330) which was followed by a second testing point two years later (n=274). Exclusion criteria were: first language other than Swedish, any diagnosis of psychiatric or neurological disorder (with exception for ADHD and dyslexia) and any vision or hearing impairment considered to affect the test-performance. Information was sent to the participants together with a consent form to be filled in by the parents (if under 18) and returned. The parents (or participants over 18) were then phoned for an opportunity to ask questions.

3.2 NEUROIMAGING WITH FUNCTIONAL MAGNETIC RESONANCE IMAGING

Study I investigated the neural correlates to IF and WM by using functional magnetic resonance imaging (fMRI). This is a non-invasive neuroimaging technique utilizing a strong magnet (1.5 tesla in Study I) and radio waves in order to detect the increases in blood flow to brain areas experiencing an increased neural activity and consequentially also an increased demand for oxygen and glucose. Haemoglobin is an oxygen carrying protein contained in red blood cells. Oxygen molecules bind to the four iron atoms of haemoglobin, transforming deoxygenated haemoglobin into oxygenated haemoglobin. The magnetic properties of iron atoms carrying oxygen differ from iron atoms free from oxygen, which are charged and thus have some magnetic susceptibility. This difference, i.e. the difference between deoxygenated and oxygenated haemoglobin, can be detected by the MRI scanner. By scanning the brain repeatedly during specific conditions (specified by the research design) the brain regions showing increased oxygenated to deoxygenated haemoglobin ratio, a consequence of a net surplus of the amount oxygenated haemoglobin delivered to regions of increased neural activity, can be detected and mapped out. This haemodynamic response in the brain (which is detected by the magnet) is referred to as the blood-oxygen-level-dependent (BOLD) signal, and is considered to be an indirect measure of neural activity.

Functional (fMRI) images can be generated with a quite high spatial resolution, with volume elements (voxels) typically representing cubes of tissue about 2-4mm on each side, which allows mapping with fairly accurate anatomical detail. However, because of the slowness of the haemodynamic response, and an acquisition time for a single brain volume of 1-4 seconds, fMRI has relatively poor temporal resolution (when compared to neural activity). This must be taken in to consideration when designing a research paradigm. The aim of fMRI studies is typically to identify neural patterns of activity that are specific to some type of information processing. Because there is always some level of activity in the brain, a baseline condition is typically included, controlling for activity unrelated to the information processing of interest. Ideally, such a baseline condition should contain all of the ingredients that the condition of interest does, except for the crucial one, e.g. memory or inhibition, thus controlling for processing of the visual stimuli, making a motor response, hearing the noise of the scanner, etc. The contrast between the two conditions thus represents the neural activity related to the function of interest.

Some of the methodological issues accompanying fMRI include scanner artifacts, dealing with noise and head movement artifacts. These problems are dealt with by preprocessing the images before statistical analyses are performed. Preprocessing steps include: realignment (motion correction with spatial matching of voxels acquired at different time points), spatial normalization (normalization of the brain to a standard template, allowing comparisons between scans and subjects), and spatial smoothing (low-pass filtering in which the value of each voxel is replaced by a weighted average of its value and the surrounding voxels' values). These preprocessing steps increase the signal-to-noise ratio, and align the BOLD images across scanning sessions and participants, thus preparing the data for statistical analysis.

There are typically two levels of analysis of fMRI data. At the single participant level, the BOLD signal is analyzed using a fixed effect general linear model (GLM) analysis with the time courses of the different conditions of the experiment entered as regressors. This means that the model attempts to attribute the changes in BOLD signal over time to the specific task conditions. The GLM is run separately for each voxel of the brain, generating separate estimates for each parameter (or condition) in the model. A high parameter estimate for a given experimental condition means BOLD (or neural activity) in this voxel is strongly associated with this particular experimental condition. For each subject, a contrast image is generated, comparing the condition of interest and the baseline condition. At the group level, these contrast images are entered in a second-level, random-effect, GLM analysis, to test which voxels show, e.g. significant increased activation in the condition of interest compared to the baseline condition. These analyses can be performed as *whole-brain* analyses, which are exploratory and necessitate correction for the multiple comparison across the large number of voxels, or with a *region-of-interest (ROI)* approach, which is typically hypothesis driven. The results can be visually presented by either superimposing the statistical maps onto high resolution anatomical images, or by listing them as three-dimensional coordinates in a standard template (e.g. atlas from the Montreal Neurological Institute, MNI, see Study I, Table 2 for an example).

In Study I the fMRI paradigm was run in a GE Signa Echo Speed 1.5 T scanner at MR-Centrum/ Stockholm Brain Institute at Karolinska Hospital. See Study I for details regarding image acquisition.

3.3 BEHAVIOURAL TESTS

3.3.1 Assessment of WM

Visuospatial WM - The Corsi block tapping task/Span board task from WAIS-R-NI (Wechsler, 1981) was used to asses visuospatial WM in Study II. This was done with sequences to be recalled and reproduced by the participants by pointing in forwards order. The task was also administered with sequences to be reported in backwards order.

A modified computerized version of this test is the Grid task (used in Study I, III, IV and V), which is a 4 by 4 grid in which a sequence of dots appear for the subject to remember and repeat (Alloway, 2007; Westerberg, et al., 2004). This was done in forward order only. This task was further tested and developed in Study III.

This task does not entail any additional manipulation of the information and should therefore, according to some definitions, be classified as a short-term memory task. We consider this a WM task for two reasons (as discussed by Klingberg, 2006) first, the sequential presentation results in formerly presented stimuli becoming distractors for subsequently presented stimuli, requiring processing to resist interference and secondly, the free recall required (rather than delayed match-response) demands a higher level of processing in that the subject must reproduce the same order allowing many possibilities to stray from the path.

In Study I the task was modified for fMRI conditions, which meant that the sequence length was always 5 dots long and followed by a number probe, e.g. 2 inquiring “if the second dot was in this box?”, requiring a yes/no response.

In Study IV, we also used the Odd One Out from the AWMA battery (Alloway, 2007) to assess visuospatial WM. This task has a higher processing load in that for each stimuli presented a judgment of the relation between the stimuli is also required. The task is to identify the odd figure out of three and to recall its location while additional sets of three figures are presented. At the end of the trial the participant has to point to the correct locations of all of the odd figures from each set in the correct order.

Verbal WM - In Study I, a visually presented sequence of 5 letters was presented for the subject to remember until a cue with one of the letters and a number inquired if that letter was presented in the order indicated by the number. This required a yes/no response.

For Study II and IV, measures of verbal WM were obtained by using a modified version of the digit span (Wechsler, 1991) using unrelated nouns instead of digits (Thorell, 2007; Thorell & Wåhlstedt, 2006). The task was to recall and repeat the sequences in the correct forward order. The test was also administered with the sequences being reported in backwards order.

Study V included the digit span from AWMA (Alloway, 2007) and sequences of digits in both forwards and backwards order were administered.

3.3.2 Assessment of IFs

In Study I we used 3 different measures of the three processes described by Barkley (1997), inhibiting a pre-potent response was measured with a Go/No-go- task (Trommer, Hoeppner, Lorber, & Armstrong, 1988), stopping an on-going response was measured with Stop task (Logan, Cowan, & Davis, 1984) and inhibiting interference was measured with the Flanker task (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999). See Methods section of Study I for details. The tasks were adapted to conform to the limitations presented in detecting BOLD signal. In both the Go/No-go and Stop task an “Odd ball” condition was added to control for the fact that no-go stimuli occurred much more seldom than the go stimuli, and since we were not interested in activation related to novelty, we added a condition that appeared as infrequently as the no-go signal which was functionally equivalent to a go signal.

In Study II, we used a Go/No-go task to assess response inhibition and used the number of commission errors (number of responses to no-go stimuli) as a measure of inhibition and the number of omission errors (missed go responses) as a measure of sustained attention. We also used an adapted version of the Day-Night Stroop Task (Gerstadt, Hong, & Diamond, 1994) to assess interference control. This version (Berlin & Bohlin, 2002) used two pairs of opposites (Day-Night and Boy-Girl).

3.3.3 Assessment of NVR

We assessed NVR in Study II, IV and V. In study II and IV, we used the Block Design subtest from WPPSI (Wechsler, 1995, 2004) in which the child had to assemble red and white coloured blocks creating the pattern presented on a card as quickly as possible. Quicker performance was rewarded with higher points.

In Study IV and V Raven's CPM or APM were used (Raven, 1998, 2003) to assess NVR. The task involved completing matrices of patterns and figures by deducing which piece out of 6 or 8 options that correctly complete the matrix.

In Study IV, we also assessed NVR with the three subtests from Leiter Battery (Roid & Miller, 1997); Repeated Patterns, Sequential Orders and Classification. Repeated patterns entailed geometrical figures organized in a pattern and required the child to continue the incomplete pattern by selecting from a set of possible figures. Sequential Orders entailed figures organized in to an incomplete progression and the task was to fill the gaps in order to complete the sequence. Classification was a matching task requiring the child to pair up figures based on a specific characteristic of the figure (e.g. shape, colour, size).

3.3.4 Assessment of Attention

In Study II we used an auditory continuous performance task from the NEPSY battery (Korkman, Kemp, & Kirk, 1998) to assess auditory attention and used the number of omissions (missed responses) as a measure of sustained attention.

As previously mentioned, we also used the omission errors from the Go/No-go task as measures of sustained attention in Study II.

3.4 TRAINING PROGRAMS IN INTERVENTION STUDIES

Study II and IV were intervention studies featuring computerized cognitive training programs. Common for all three programs (IF, WM and NVR programs respectively) was an adaptive algorithm, allowing training at the capacity limit of each child. The procedures were also the same in that children trained around 15 min/day, 5 days/week for 5-6 weeks. The children were presented with the training program and asked if they wanted to play for a little while every day and if they agreed (which they all did) they were presented with a schedule were they should place a sticker for every day they had played. Five stickers would be rewarded with a small gift such as a car, small book or bubble blowers. At the end of the study, they were also given diplomas and either gift vouchers or 500 SEK for their participation. For Study II, the training was supervised by the researchers at the preschools and in Study IV the children were supervised by their parents at home. The compliance and progression of the training was in turn, supervised online by the researchers and feedback on the training was given via email or telephone once per week.

3.4.1 WM training program

The visuospatial WM training program used was essentially the same in both studies and was age adapted by Cogmed Systems and based on their previous WM training paradigms (i.e. Robomemo) (see Figure 2 for examples). We chose to focus exclusively on visuospatial WM based on the higher associations reported between visuospatial storage and NVR compared to verbal storage and NVR (Kane, et al., 2004). There were five versions of the task in Study II and seven versions in Study IV. The WM tasks were all span tasks with sequential marking of the Munchers (by changing colour, jumping and making a sound) for the participants to repeat by clicking on the Munchers in the correct order. Difficulty was adjusted by increasing the length of the sequence to be remembered.

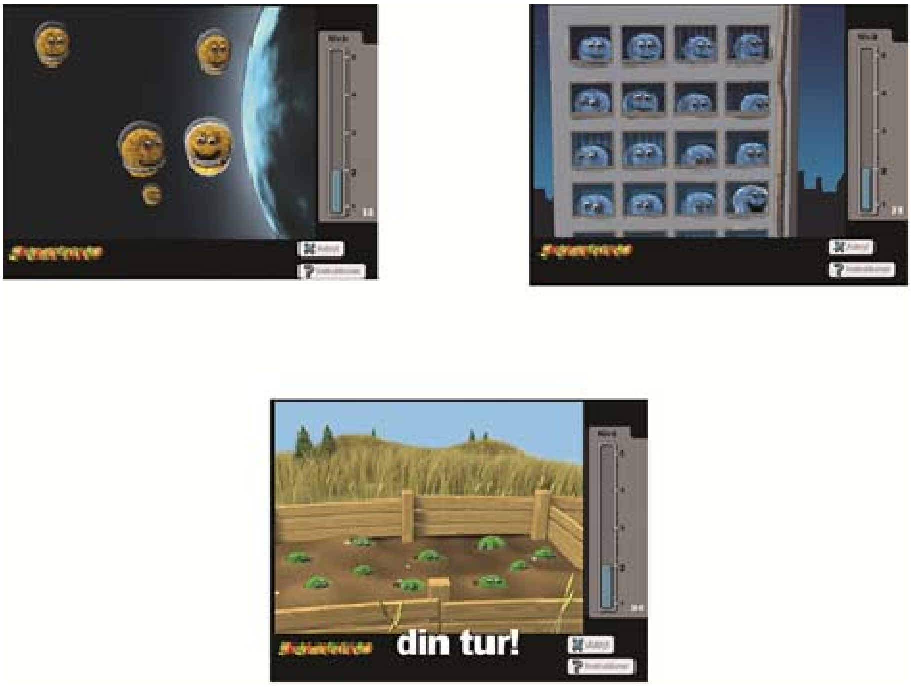


Figure 2. Examples of the WM training tasks illustrating Munchers in different environments. The task is to view and try and remember a, by the computer, marked sequence of Munchers and click on them in the same order. All tasks use the same algorithm adopting the length of the sequence to remember according to the performance level.

3.4.2 IFs training program

The training program targeting IFs in Study II included the three core inhibition tasks also used as tests in Study I, Go/No-go, Stop task and Flanker task (see Figure 3 for examples) and was developed together with Cogmed systems. There were two versions of the two response inhibition tasks, differing only in appearance and one version made of the Flanker task (meant to train interference control). The tasks consisted of a character called the Muncher, who loved eating fruit that appeared on the screen prompting the Muncher to jump to fetch the fruit. The fruit was thus the Go-stimuli and the No-go and Stop signal was a fish skeleton, disliked by the Muncher, thus requiring an inhibition of the jump. The difficulty was adjusted for the Go/No-go task by decreasing the time allowed to respond. The challenge with the Stop-task is the initial presentation of a go-signal that sometimes changes in to a stop-signal. Difficulty was adjusted by changing the time between the go-signal and the stop-signal, shorter intervals leading to easier disruption of the on-going response. The Flanker task simply had five Munchers holding a sign each with an arrow pointing either left or right. The child had to respond only in accordance with the central sign, thus inhibiting interference from the surrounding stimuli.

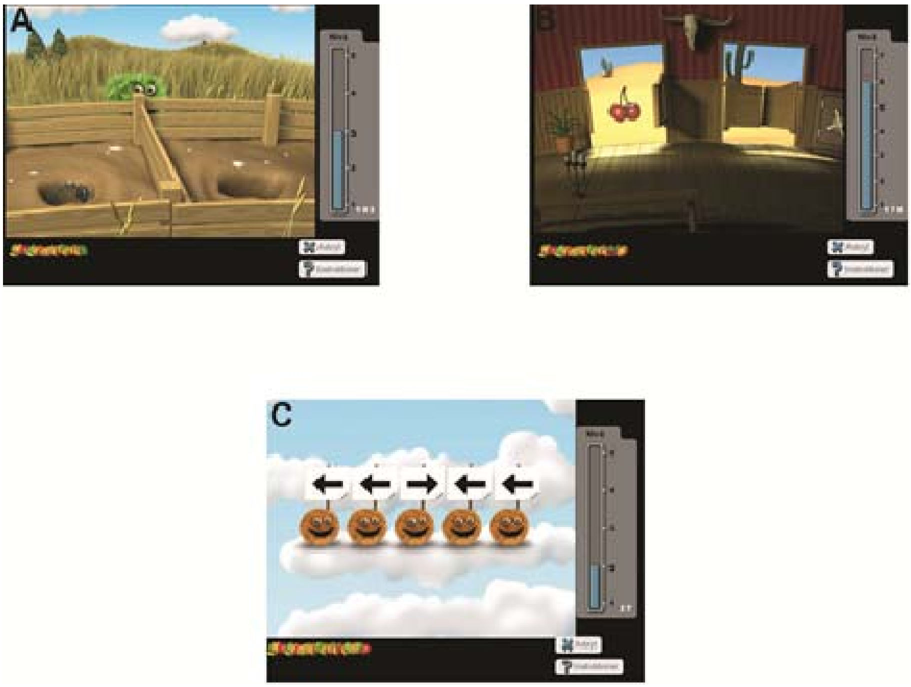


Figure 3. Examples of the three IFs training tasks from study II. The top left screen (A) shows a Go/No-go task with a right/left response choice. The little green “Muncher” should remain still when a fish is displayed in one of the pits and jump when a fruit is displayed. The top right screen (B) shows a Stop task which, similarly to one of the Go/No-go tasks has a right/left response choice. The difference here is that the initial cue is always a fruit (go) which sometimes changes into a fish (stop-signal), warranting a stop of an already initiated respone. The cental frame (C) shows the Flanker task in an incongruent trial, showing conflicting information between the central (and response governing sign) and surrounding signs.

3.4.3 NVR training program

The NVR training program used in Study IV was developed specifically for this purpose. The program was based on the three tests from Leiter Battery (Roid & Miller, 1997) that were shown to load highest on fluid intelligence (SEM reported in the Manual). The tasks were Repeated Patterns (RP), Sequential Orders (SO) and Classification (CL) as described in the test section above (see Figure 4 for examples). Some steps were taken to adapt the test items in order to develop automatically generated items, including removing all semantic objects from the items and restricting them to geometrical figures.

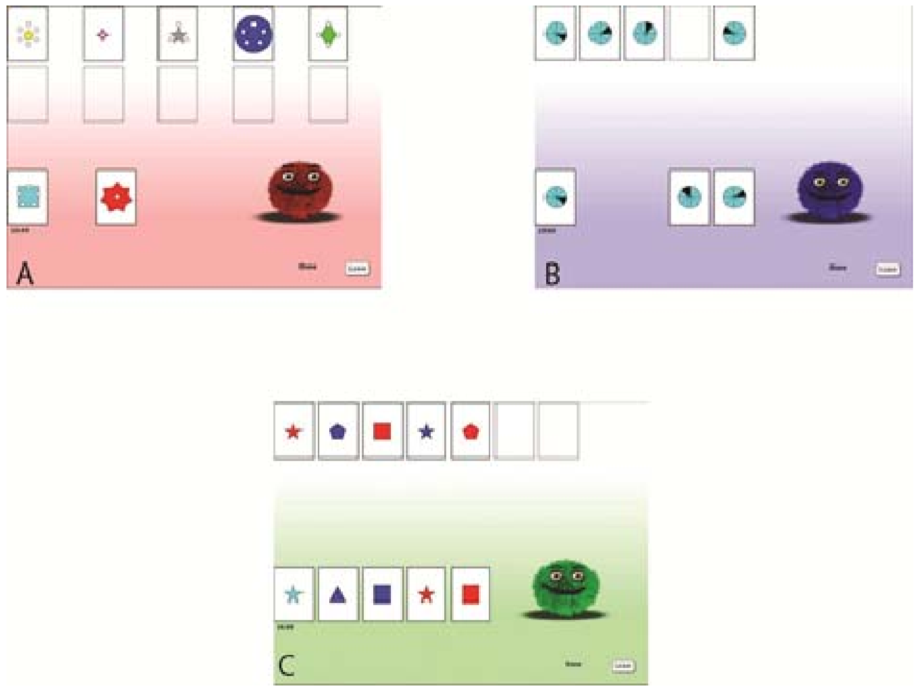


Figure 4. Illustration of the three NVR tasks in the training program. The top left screen (A) shows a more advanced level of the CL task where the task is to match the two bottom cards to two of the top row cards based on the same principle. In this example the principle is number of dots in the figures. The top right screen (B) shows a SO trial, requiring the child to select one of the cards on the bottom row in order to complete the sequence in the top row.
The bottom figure (C) shows a more difficult trial of the RP where the child has to identify the pattern in the top row and select two cards from the bottom row in order to repeat the pattern.

The development of the training program started with identification and extrapolation of the rule systems in the tests. Examples of the rules could be: number of distractor cards, number of cards in a pattern, number of open slots to be filled etc. This was followed by programming the rules in order to generate many items differing only on surface features (e.g. colour, shape size etc). This was followed by two pilot studies in which a sample of 4- (n=17, Pilot 1) and 6-year-olds (n=12, Pilot 2) were tested on the items developed, along with the original Leiter tests, another NVR test (Block Design) and a WM test (Grid task). After the first pilot item performance was modelled using a type of Item Response Theory (IRT), Rasch analysis (Rasch, 1960), ordering the items according to difficulty. Next, we wanted to ensure that the items were difficult for the "right reason", i.e. NVR related as opposed to perceptually or WM related for instance. In order to identify which factors/ rules that contribute to item complexity the relation between load on these factors and NVR ability and WMC we performed additional analyses. For each of the three tests, we ran backwards multiple logistic regression analyses with the probability of passing an item (pass/fail) as dependent variable and the load on each of the specific rules (e.g. number of distractors being 1, 2 or 3), a composite NVR score (from principal components analysis of the NVR measures), WM score, interaction terms with the rules and NVR and WM respectively and age included in the models as independent variables. The variables that remained in the final models thus significantly predicted the probability of passing each item and the interaction term with NVR ensured that items were difficult in NVR-related way. This allowed us to focus our difficulty adjustment on the rules related to NVR ability compared with WM or visual perception related difficulty. Additional items were created accordingly which were then tested in the second pilot along with the items obtaining less than 0.5 in success rate from Pilot 1. The items were then analysed with Rasch methods again (see Figure 5 for an example) and organized after hierarchy of difficulty.

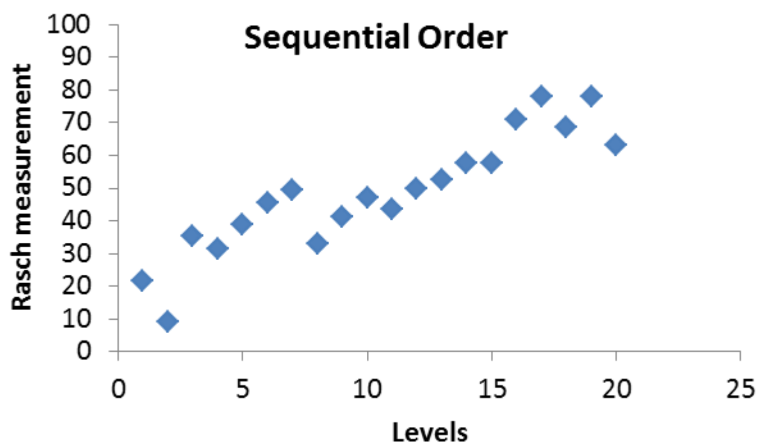


Figure 5. The graph shows the hierarchy of items in the Sequential Order task according to the Rasch measurement obtained for each item. This is clearly not the best order and levels were subsequently reorganized to follow a progression based on difficulty.

3.4.4 Active control programs

When designing intervention studies it is important to select an appropriate control condition to compare your active condition with. This should preferably be as similar to the real condition as possible, bar the active ingredient. This is well established in fields with a longer tradition e.g. placebo controlled pharmacological studies, but is unfortunately not yet common practice in the field of cognitive training (Klingberg, 2010; Sternberg, 2008). This is crucial when comparing conditions, as expectancy and motivational effects on performance on intelligence tests have been well documented (Dickstein & Kephart, 1972; Oken et al., 2008). For this reason it is equally important, however sometimes difficult, to have participants blinded to the interventions.

Study II included an active control group that played a commercially available computer game called “Björnes magasin”. The tasks (see Figure 6) were selected based on their perceived low load on WM and IFs. This training was conducted with the exact same procedure as the actual conditions, including the motivational stickers and gifts etc. This condition controlled for the enhanced computer skills (using the mouse), individual time with an adult and receiving special attention. Since the training was performed at the preschools and the children talked to each other about their traning, we would not have been able to keep the participants and teachers blinded to the conditions if completely randomized so we prioritized to keep them blinded in this study.

Figure 6. Examples of the active control program included in Study II. The top left screen (A) involved popping the bubbles released from the hose and the top right screen (B) involved protecting the planet in the center from collision with flying objects by moving the mouse and redirecting them. The bottom screen (C) involved clicking with the mouse on the tins where a puppet appeared before they disappeared.

In Study IV we raised the ambition level with placebo controlled conditions further and decided to let the control group perform the actual active conditions with the only difference being the individually adjusted algorithm remaining constant, randomly selecting items from the bottom three levels. This has been done previously in WM studies where it has been shown that one of the key factors resulting in effects is training close to the capacity limit (Klingberg, et al., 2005; Klingberg, et al., 2002b). This has however, not been done for NVR training, where a different set of rules governing the mechanisms of training may apply. The placebo condition trained the same tasks as the combined group, training both WM and NVR, but remained on levels with only one stimulus to remember for WM and levels with only the basic principles of NVR (e.g. limited number of answers to choose from etc.).

4 RESULTS

4.1 STUDY I

Study I examined the neural overlaps in brain activity between tasks tapping IFs and WM. We used the previously described Go/No-go, Stop task and Flanker tasks to assess IFs, a verbal and a visuospatial task to assess WM. In the Go/No-go and Stop tasks, a modification to the normal task designs were made in order to control for the novelty effect associated with the less frequent no-go trials. These Odd ball trials required a go-response, i.e. a button press, and were used as the contrast to the No-go/Stop trials.

The behavioral results showed satisfactory levels of accuracy and reaction time patterns on the main outcomes meaning; significantly lower accuracy (t= 3.33, *d.f.*=13, $p <$ 0.005) and longer reaction times for the incongruent Flanker trials compared to the congruent trials (t = 8.49, *d.f.* =13, p <0.001), a stop signal reaction time of 166 ms for the Stop task, 9% commission errors on the Go/No-go task, 88% accuracy on the spatial WM task; 91% accuracy for the verbal WM. Significantly longer reaction time was observed for the odd ball trials compared to go and control trials in both the Go-/No-go (t = 4.14, *d.f.* =13, p < 0.005) and Stop task (t = 5.65, *d.f.* = 13, p = <0.0005).

Whole brain analysis

For each task, events were modeled with the haemodynamic response function and the task's timing specifications to produce contrast images. For each task, separate regressors corresponded to each condition of the task (e.g. go-trials, no-go-trials and odd ball for the Go/No-go task). This resulted in 5 contrast images for each participant, which were further analyzed in a group level analysis of random effects. These images were entered into a within-subjects ANOVA. The results for each task are listed in Table 2 in Study I.

Valid conjunction inference (meaning that each contrast is significant independently, as proposed by Nichols in 2004) of significant activity in overlapping areas between tasks was employed, both within domain (IF and WM respectively) and between domains. Results from the whole brain analysis showed overlapping activity for the Go/No-go, Stop task, visuospatial WM and verbal WM contrasts in right inferior frontal gyrus (extending in to the insula). The mean relative signal change in this area for each contrast respectively is shown in Figure 2 in Study I. Further domain specific overlaps were seen for the WM tasks in bilateral frontal and parietal regions and in bilateral inferior frontal gyrus and right superior/middle frontal gyrus between the Go/No-go and Stop task. No significant conjunction between all three inhibition tasks was detected. Mean relative signal change in the overlapping regions for each task condition was not correlated with behavioral performance for any of the regions or tasks.

Region of interest analysis

In order to assess the neural underpinnings of the functions at a closer range, ROIs were generated from the results from the whole brain analysis. Twelve ROIs were selected for further investigation and mean relative signal change associated with each task contrast respectively are shown in Figure 4 of Study I. In order to investigate possible conjunctions not reaching statistical significance in the whole brain analysis, we performed (small volume corrected) conjunction analyses for each ROI. Significant commonalities between all five tasks were shown in the right inferior frontal, right middle frontal and the right parietal cortex. The Flanker task was the only one that showed a significant correlation between the task activity (incongruent vs. congruent) and reaction time difference between the two conditions in the right inferior frontal, indicating that greater activity was associated with more efficient interference control/inhibition in this region.

Conclusions

The main findings were thus, that there are commonalities in the neural underpinnings of IFs and WM. These overlaps include the right inferior frontal gyrus, right middle frontal gyrus and right parietal brain regions. More commonalities were seen between the WM tasks and the response inhibition tasks than between WM and the Flanker task, and response inhibition and the Flanker task, as will be discussed.

4.2 STUDY II

Study II aimed to investigate if it was possible to improve EFs in a preschool sample. This was done with intensive computerized training on tasks tapping IF or WM respectively. The tasks used to train WM (described in the methods section) were exclusively visuospatial in nature. The IF training program consisted of the Go/No-go, Stop task and Flanker task. In order to control for test-retest effects we included a passive control group. Additionally, we included an active control group that played commercially available games (previously described) and in order to assess general intervention effects. There were however no significant differences in performance improvements between the control groups and they were therefore pooled in the group effect analysis. ANCOVAs with the difference score (T2-T1) as dependent variable, group as main factor and age and sex as covariates were run for each of the tests (details in Table 1 of Study II). Post hoc analysis comparing the actual trained groups with the pooled control group showed that WM training increased performance on non-trained WM tasks, such as the Span board test and Word span test. The WM group also showed significant improvements compared to controls on measures of sustained attention as measured with a continuous performance task and the number of omissions made on a Go/No-go task. Analyzing level reached on the trained tasks on the last three days compared to day 2-4 showed a significant improvement on all of the WM tasks (as tested with a paired t-test).

The training targeting IFs did not show any significant improvements on either non-trained tests of IFs, WM or attention. The analysis of the trained tasks did, however, show a significant improvement on two of the three tasks, i.e. the Go/No-go and the Flanker tasks. This meant that they were able to perform with sustained accuracy quicker at the end of the training than at day 2-4.

Conclusions

The results showed that it is possible to improve WM capacity in preschoolers using a targeted computerized intervention program. WM was improved across modalities even though the training program was exclusively visuospatial in nature. Transfer of the training effects was also seen for two measures of sustained attention. Training of IFs, however, did not lead to significant improvements on IFs, WM or attention.

4.3 STUDY III

The third study in this thesis was a methodological experiment aimed at improving the precision of which WM can be assessed in the lower capacity ranges. The Study was performed in a stepwise manner firstly examining the variability in the Grid task on 4- and 6-year old children (Experiment 1), selecting items (based on IRT and logistic regression analysis) to be tested and validated against another WM test in a separate sample of 4- and 6-year olds (Experiment 2).

Experiment 1

Items were selected from a large database with success rates on trials used in WM training. Items were chosen so that three hypothesized difficulty levels consisting of the same number of stimuli/dots would be created. These items were tested in a sample of 4- and 6-year-olds and in accordance with our expectations, the results showed a large variability even though they consisted of the same number of dots. The performance on 84 items evenly distributed over levels 2 to 5 was analyzed using an IRT model (Rasch analysis) which enabled us to rank the items based on difficulty. The Rasch model generates an item difficulty score on an interval scale as well as person ability score along the same scale. This allows parallel ranking of items and individuals along the same axis and effectively illustrates each item's distinguishability between individuals. The test showed high internal reliability and indicated measurement of one underlying construct.

In order to identify the system determining the difficulty of the items we ran forward multiple logistic regression analysis with the subject's response to each item as dependent variable, and the characteristics constituting each item as independent variables. We also added a constant to the null model and a person factor, controlling for all of the individual differences not of interest (age, sex, motivation etc.). The factors significantly predicting performance on items were: number of dots (level), mean distance between dots in an item, mean number of side positions of an item, mean number of times the pattern line crossed itself, and mean number of times a dot was followed by another dot on the same axis as the previous one (see Table 1 for regression coefficients).

	B	SE	Sig	Exp (B)
Constant	5.04	0.56	<0.001	154.64
Dots	-1.53	0.12	<0.001	0.22
Distance	-0.42	0.10	<0.001	0.66
Side positions	-0.48	0.20	0.02	0.62
Crossings	-0.63	0.61	0.01	0.20
Same axis	0.77	0.29	0.01	2.16

Table 1. Regression coefficients from the final model from forward multiple logistic regression analysis. It also included one parameter for each person (n=37) which were included to control for individual differences predicting performance but were not of interest and therefore not listed here.

Combined with the results from the Rasch analysis we let these results guide the selection of items to be organized by difficulty into two sub-levels within each former level (consisting of the same number of dots). Figure 3 in Study III shows the way in which these items were selected. Three items for each sub-level which had shown a satisfactory uniform distribution from the Rasch analysis as well illustrated a close fit to the predicted values from the logistic regression analysis, were selected.

We showed in another series of logistic regression analysis that the new sub-levels were clearly separable from each other and at the same time, uniform in difficulty within them and that this organization explained more variance in the data than when grouping the sub-levels in to one (old) level.

Experiment 2

The selected items were then tested in a new sample of 4- and 6-year-olds along with a separate WM test, the Odd One Out (AWMA, Alloway, 2007). This was done to validate that the Grid task tested what it was intended to test, namely WM. Performance on the Grid task was analyzed with the Rasch model confirming the item's organization into separable sub-levels (as seen in Figure 3B in paper from Experiment 1). Correlation with the Odd One Out was high (r = 0.83) validating the construct aimed to be measured.

Conclusion

The results showed that for the Grid task, there was a great variability in difficulty within a level consisting of the same number of items. The items were ranked and the difficulty explained in terms of which factors that predicted the difficulty level. Based on this information, a subset of items were selected, organized in to sub-levels and tested along with another WM test, on an independent sample of children. Performance on the items indicated that the new sub-levels were stable and separable. The new test showed high separation ability between individuals, satisfactory internal consistency and was validated against the other WM test.

4.4 STUDY IV

Study IV investigated whether it is possible to improve Gf in a sample of 4-year-olds with training on computerized NVR tasks. The study was designed to investigate the interrelation between WM and NVR in terms of whether training effects on one construct would transfer to the other. Four randomly assigned groups participated in the study training either WM, NVR, a combination (CB) or a placebo controlled (PL) condition. The neuropsychological testing before the training began showed that there was no difference between groups on any of the tests or background information variables (e.g. sex, parental education). After the 5 weeks of training, the results showed a significant group difference on several tests as analyzed with ANCOVA.

Gf was assessed as a latent variable consisting of Raven's CPM's subtests A, AB and B, and Block design. Gf score at T2 from the latent model was entered as dependent variable, with group as fixed factor, age and Gf score at T1 (from latent model) as covariates. The results showed that there was a significant group difference on Gf, and post hoc T-tests (unpaired, two-tailed) revealed that the NVR group had significantly larger improvement than the PL group. Table 2 of Study IV consists of the means and standard deviations on all the tests, as well as standardized change for the training groups respectively. As expected, the NVR and CB group both improved significantly on the test most similar the trained tasks, the Leiter tests (called trained tests in the paper). There was no group effect on the total score of Raven's CPM but since the scores between subsets seemed to differ, they were split (as suggested by the manual) into sets A, AB and B. There was then a significant group effect for set B, which proved to be caused by the NVR group significantly outperforming the PL group. A similar effect was seen for Block design. Raven's CPM and Block design are transfer tests *within* construct for the NVR training groups.

Assessment of the memory domain revealed expected training effects for the WM and CB group on the test similar to the trained tasks, the Grid task (trained test in the paper). There was also a significant group effect in the Odd One Out and post-hoc tests showed that all three active conditions (the WM, CB and NVR) improved on this test (trend for NVR). This indicated a transfer *within* construct for the WM and CB group but *between* constructs for the NVR group.

An additional analysis was performed after the paper was accepted to assess whether the training effects on tests with different processing demands could be distinguished. An ANCOVA was run with Odd One Out (T2) as dependent variable, group as fixed factor, and age, Odd One Out (T1) and the difference score on the Grid task (T2-T1) as covariates. We thus assessed the improvements in the component that differs between the Odd One Out and the Grid task and the results showed a significant improvement in the WM group (p = 0.038) (and a trend in the CB and NVR groups ($p < 0.1$). This indicates that the domain general processing component (central executive) of WM was trained even though the WM training relied on tasks with lower processing demands.

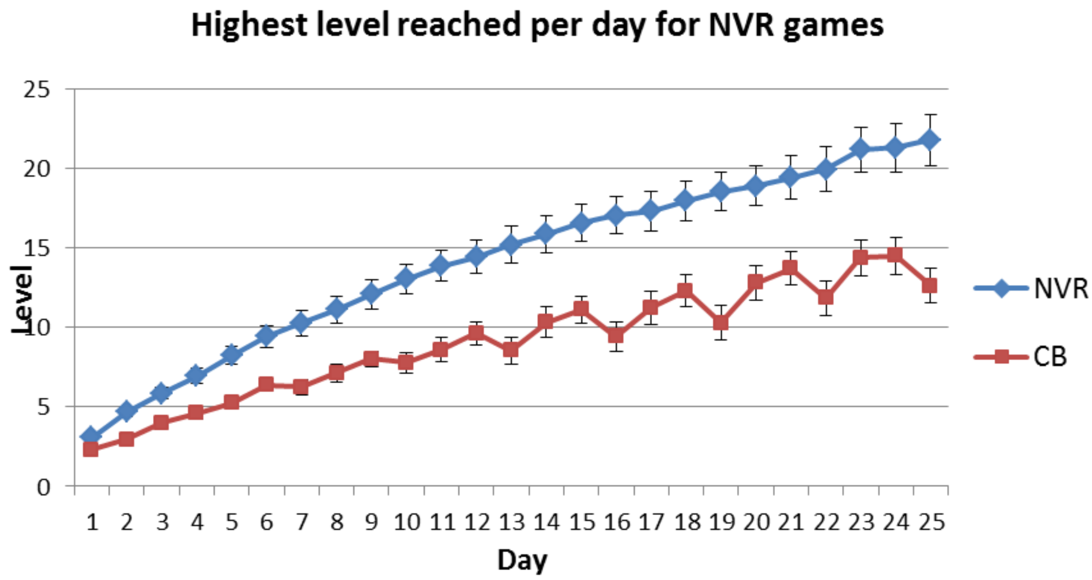
Effects on the verbal memory test, the Word span, did not reach significance. However, since we did see such as effect in Study II, we performed a guided post-hoc test between the WM and PL group which did show a marginally significant effect (p = 0.05, one-tailed t-test). This modest effect led us to question if the low load on the training program in the PL group had in fact been enough to train their WM. When substituting the control groups from Study II with the PL group for this analysis, results showed a significant training effect for the WM group (p = 0.007, unpaired t test, two-tailed). This could mean that the PL group in Study IV actually trained WM (and NVR) to a small extent which will be discussed later.

One of our aims was to investigate whether training both NVR and WM together would lead to any improvements beyond what could be expected, in other words, if there would be an interaction effect between NVR and WM caused by the combined training. This was investigated with linear regression models with the different groups coded based on the amount of training they received of each construct. The dependent variable was the test score at T2, the constructs (WM, NVR and an interaction term WM x NVR) were independent variables along with age (see Study IV, page 7 for details). This controlled for the fact that the CB group only received half as much training on each construct as the WM and NVR groups respectively. The results showed interaction effects for two of tests, the Leiter test and the Grid task. This illustrated that the effects on the trained tasks and consequentially also the trained tests was not proportionate to the amount of training received, but showed similar effects for both active conditions for each construct respectively. The results did not show any additional interaction effects on any other tests but confirmed the main findings from the previously reported ANCOVAs (see Table 3 in Study IV).

Additionally, we investigated the possibility of different baseline performance leading to different training gains by looking at the interaction between group and baseline performance (T1 x Group). There were no significant interactions for any of the tests, indicating that baseline level did not determine the degree of training effects for any of the tests. Similarly when investigating effects of sex; there was no significant interaction between sex and group.

Trained tasks

The training improvements on the trained tasks indicated that the active groups all improved significantly when looking at the average level of the best two days compared with the average of day 2 and 3 (all $p < 0.05$ for all tasks and all three groups).



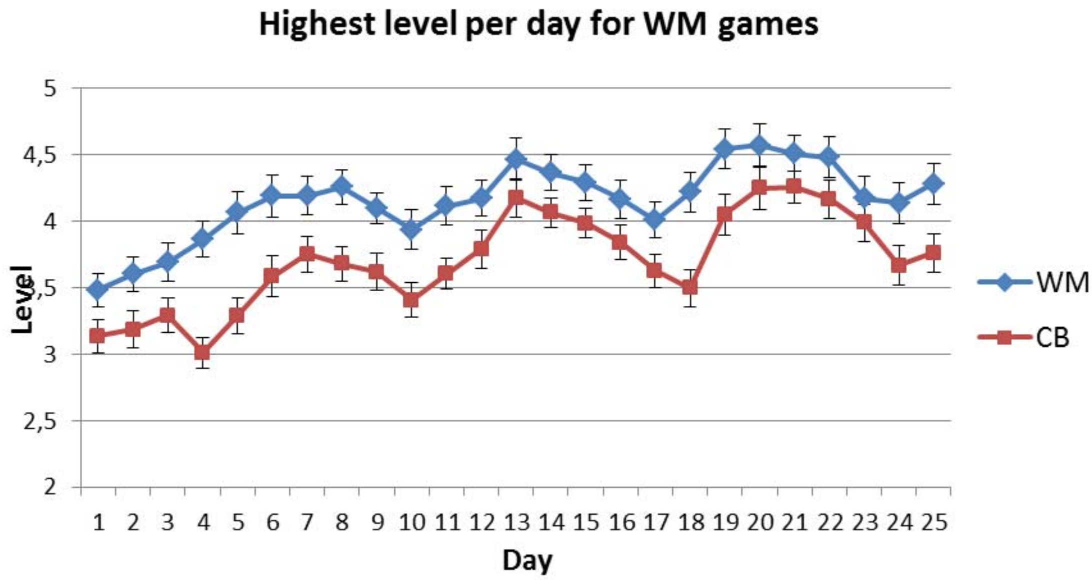


Figure 7. Training curves for the training groups on the NVR training tasks above and the WM training below. The groups training only one construct (NVR and WM respectively) is depicted in blue whereas the CB group is in red.

Conclusion

The results showed that it is possible to improve Gf with computerized training on NVR tasks in 4-year-old children. Training effects transferred to non-trained measures of NVR as well as a tendency to transfer between constructs on a WM test. WM training led to improvements on other WM tests but not to tests of NVR. The CB group improved as to be expected on the tests but did not show any interaction effect from training both constructs within the same regime.

4.5 STUDY V

The last manuscript aimed to investigate the effects of music practice on the development of cognitive functions, WM and NVR in particular. This was done in a longitudinal study investigating a developing population (aged 6 to 25) twice, two years apart. The parents of the under aged subjects and the subjects over 18 years of age filled out questionnaires on extracurricular activities and socioeconomic background. They were asked if they played an instrument (yes/no), if so, which instrument and how many hours per week they practiced. They underwent neuropsychological assessment which included the Dot matrix (a version of the Grid task), the digit span and Raven's APM (see raw scores in Table 2). Participants were categorized depending on whether they played any instrument or not (binary category) but also whether they played an instrument that required musical notation reading from one or two staffs (resulting in three categories). There was no effect of parental education level or sex on music category. There was also no effect of the amount of practice/week between the two music groups. Linear regression analyses with the test score at T2 as dependent variable, age, sex, test score at T1 (thus holding the differences at T1 constant when analyzing performance at T2) and binary music category at T1 showed a significant effect of music category for the Dot matrix and the Raven's APM, but not for the Digit span. The same pattern, including the null results for the digit span, was observed when using the ternary music category. The Digit span test was therefore not investigated further. The model using music as a ternary category provided a slightly better fit to the data.

Test	Music category	T1 ***M* (*SD*)**	T2 ***M* (*SD*)**
Dot matrix	No instrument	25.1 (7.5)	27.6 (7.2)
	Single-staff	26.3 (5.9)	29.7 (8.1)
	Dual-staff	26.9 (5.6)	31.5 (6.3)
Raven	No instrument	-0.31 (0.71)	-0.065 (0.68)
	Single-staff	-0.10 (0.58)	0.18 (0.58)
	Dual-staff	0.10 (1.10)	0.43 (0.98)
Digit recall (back)	No instrument	13.9 (5.6)	15.9 (5.5)
	Single-staff	13.5 (4.0)	15.3 (3.4)
	Dual-staff	16.5 (7.2)	17.5 (6.9)

Table 2. Means (*M*) and standard deviations (*SD*) for the three outcomes for each music category for the first and second measurement points (T1 and T2).

Backwards linear regression models were fitted with the following additional covariates: hours spent online or gaming per week, hours spent on physical activity per week, hours watching TV per week, father's education level and mother's education level. Both ways of classifying music were also entered allowing the statistics program to choose the one explaining more variance in the outcome variable (see regression coefficients for model but with forced entrance for all variables, selecting music as a ternary, in Table 2 in Study V).

We also analysed whether time spent on music practice per week could explain the performance at T2 better than music category alone. Adding the time variable to the model in Table 2 showed a significant increase in fit for the Dot matrix, but not for Raven's APM.

Next we analysed whether the music effect on one of the constructs was indirectly affecting the other (through mediation). This was done by adding the T1 score and the improvement score (T2-T1) for the other construct when analysing the first construct (respectively). The results showed that even though the change in performance in the other outcome also explained performance at T2, music category (as a ternary) still remained marginally significant for both constructs, interpreted as a direct effect from music practice to each of the constructs independently. The best fitting model explaining Dot matrix performance at T2 consisted only of Dot matrix at T1 and music h/week and the best model for Raven performance at T2 consisted of Dot matrix at T1, change in Dot matrix between T2 and T1 and music as a ternary category.

Conclusion

This study investigated the effect of music practice on the development of WM and NVR. The results showed that the amount of music practiced per week significantly explained performance on WM, two year later and that which type of instrument played best explained performance on a NVR task at the later time point. Both constructs seemed to be affected (at least in part) directly by music practice.

5 DISCUSSION

The results will be discussed beginning with Study III as it addresses a methodological issue rather than relations between abilities. Next, Study I will be discussed in relation to other neuroimaging findings related to WM and IFs, after which a section will follow discussing these findings in relation to the training results from Study II. The training results will initially be discussed in isolation for WM (Study II and IV), IFs (Study II) and NVR (Study IV) respectively, and subsequently together in a general discussion on cognitive training and transfer. Finally, a discussion on cognitive training effects from music practice will be included followed by general concluding remarks.

5.1 STUDY III AND METHODOLOGICAL ISSUES IN STUDIES ON DEVELOPMENTAL SAMPLES

This study investigated a methodological concern with the usage of span tasks in developing samples. Span tasks have been argued to be preferred when studying developing samples since the same task can be used across all ages (Gathercole, Pickering, Ambridge, et al., 2004). This is a valid argument; however the relative increase between levels differs and is especially gross in the lower ranges. This has been an overlooked aspect in developmental studies and may underestimate the variance in cognitive abilities in the lower capacity ranges. This study aimed to investigate whether sub-levels within a level consisting of the same number of stimuli could be justified in a systematic way. Experiment 1 illustrated the issue of great variability within the levels and identified the factors that predicted the difficulty level of the items. A sub-set of items was then selected complying both to the general difficulty ranking and the model with the complexity factors explaining the difficulty. The distribution was then verified in an independent sample of children. The final items are enclosed in the article with a proposed scoring system which proved to be highly correlated (r = 0.86) with the ability score obtained from the Rasch-analysis. This sub-division of levels increases the probability of distinguishing between individuals and should provide a more exact measure of WM ability. The possible added predictive value of our modifications is not investigated here but would be interesting to determine.

The issue of comparing individuals across different abilities and ages is perhaps not resolved by this study, as the problem with uneven advancement in difficulty between levels (consisting of different number of stimuli), remains. However, developing sub-levels for all levels and using it for all ages/abilities would allow a more precise measure across the board. Difficulty adjustment is an intricate question and is especially important in the study of developing populations as many of the queries investigated involve identification of differential trajectories of abilities etc. These types of conclusions may be confounded by relative load injustices between levels when using span tasks across different ages. Discrepancies between reported findings are commonly discussed in terms of differences between task specifications, suboptimal difficulty adjustments and different age groups assessed etc. and while these are legitimate explanations, perhaps more could be done to improve such methodological insufficiencies. This study represents one such attempt and will hopefully be used and further developed to obtain better separation between individuals in measures of WM.

5.2 STUDY I AND REPRESENTATION OF OVERLAPPING NEURAL ACTIVATION

This study aimed to investigate the commonly activated areas between performance of IFs and WM tasks. The design aimed to tap these functions separately in order to distinguish the neural correlates of each domain (IFs and WM respectively) and of common functioning between domains. Previous studies have identified the right inferior frontal gyrus at the core of response inhibition (for recent reviews see Aron, 2007; Chambers, et al., 2009; Mostofsky & Simmonds, 2008). Recent fMRI studies have provided evidence that this area has a general inhibitory control function suppressing also speech, manual and oculomotor response (Leung & Cai, 2007; Xue, Aron, & Poldrack, 2008). Even though the tasks used were selected to measure either IFs or WM, avoiding interaction between the two, the inherent relation between the two functions make that virtually impossible. Taking a closer look at the tasks in our study, one can discuss the relevance of a common response inhibition component in all of the tasks, including the WM ones. If there is ever more than one response selection to make, inhibition of the non-selected ones must be performed (Mink, 1996). This is the case in the active WM condition but not in the control, where the participants always respond in the same way. This is also the case in the Flanker task where a right or left response is required thus, selecting one response while inhibiting the other motor response. However, this is the case also for the congruent trials, why this effect is controlled for in the contrast for this task. This may explain why the Flanker task did not share common neural resources (in the right inferior frontal gyrus) with the other tasks to the same extent in the whole brain analysis.

The results from this study show that there are commonly activated areas for IFs and WM functions. Whether this overlap represents a limited shared resource pool or not is beyond the scope of this study. However, evidence from studies manipulating WM demands in inhibition tasks have found impaired inhibition performance with greater WM load (Roberts, Hager, & Heron, 1994; Van der Stigchel, 2010), perhaps indicating limited shared neural resources. Activity recorded while performing such tasks has been reported in bilateral inferior frontal regions, left inferior parietal, left middle frontal (Kelly, Hester, Foxe, Shpaner, & Garavan, 2006) and left PFC (Smith & Jonides, 1998). However, untangling the effects of probable interactions between domains is not possible from this type of paradigm.

This study was able to find overlapping brain areas for IF and WM using several different tasks within the same participants. This indicates common neural processes between the two functions that supersede the differences in task demands both within, and between domains.

5.3 STUDY I, II AND IV AND COGNITIVE TRAINING EFFECTS

The cognitive training studies in this thesis focus on repeated performance on tasks presumed to tap a specific ability and aim to actually push the boundaries of the capacity limits. This differs from approaches where strategies are taught to alleviate strains on the functions and has been suggested to provide more transfer effects than strategy training efforts (Morrison & Chein, 2011). This has been discussed in terms of training processes underlying a function that may be common to other tasks as well allowing improvements otherwise limited by task specific strategies.

5.3.1 Effects of WM training

Study II aimed to investigate if it was possible to improve EFs in a preschool sample and this was deemed successful in the WM domain but not for the IFs. WM was improved across modalities even though the training program was exclusively visuospatial in nature. This indicates that domain general aspects of WM were trained. As previously described, the domain general components of WM are usually assigned the central executive. This either indicates that training affected the supposed central executive component of WM or that the storage components are not as domain specific as previously supposed, at least at this age. The results from Study IV support that training affected processing components of WM as significant improvements were seen on a task with a high processing load, the Odd One Out. This was further substantiated by analyzing the improvements on Odd One Out while controlling for the improvements seen on Grid task. In this analysis the improvement on the Odd One Out was still significant for the WM group, suggesting that training led to improvements in components beyond the task specific ones. This indicates that the type of tasks used in the training (simple visuospatial span tasks with sequential presentation of stimuli), at least for this age group, tap not only storage components but also depend on domain general processing resources, as previously reported (Alloway, et al., 2006).

Further support for this comes from Study II where it was found that WM training effects also transferred to measures of sustained attention seen as fewer omission errors (on an auditory continuous performance task and on the go-trials of a response inhibition task). These findings corroborate the notion that WM training affects general attention processes, which has been proposed to be the main determining factor underlying both development and training improvements of visuospatial temporary memory systems (Astle, Nobre, & Scerif, 2010).

5.3.2 Possible transfer mechanisms

The mechanisms that determine if cognitive functions can be trained and to which other functions effects will transfer, are still not clear. One approach suggested to predict transfer is to look at overlapping brain areas of activity between trained tasks and transfer tests (Olesen, et al., 2004) as attempted in Study I. Since overlaps between IF and WM were identified (primarily in the right inferior frontal gyrus), we hypothesized that training effects would transfer in both directions. Previous WM training has shown effects on a Stroop task (Klingberg, 2002b; 2005, Chein, 2010), however, the exact nature of this effect is unclear and may be specific to improved interference control, rather than response inhibition (as only incongruent trials were used in the Klingberg studies). Regardless, such transfer effects were not seen on either a Stroop task or a Go/No-go task after training WM in Study II. The reasons for this could lie in the different ages investigated in Study I and II. As different EFs develop at different paces, one might expect that transfer effects differ because of these changing interrelations. Similarly to Study I, the previously reported transfer effects from WM training to IFs, were all on older individuals (aged 7-15 in Klingberg 2002b, 2005 and 20 year-olds in Chein 2010).

An alternative proposal for when transfer occurs was presented by Dahlin and colleagues (2008), who suggested that transfer occurs after training of updating only if the striatum is commonly activated between training and transfer tasks. This region was not one of the overlapping areas between IFs and WM tasks as seen in Study I, and our results could thus fit with such a theory.

5.3.3 Possible explanations for lack of effects after training IFs

The way in which the training regime was designed may have been flawed. It may be that difficulty was not optimally adjusted, and that the time targeting the key component of inhibition was insufficient. Jaeggi and colleagues (2008) showed a dose-response pattern for the transfer effects in dual-updating training and similar effects were found from time spent on music practice to WM in Study IV. Even though these results were for WM, it is possible that IFs also respond to dose with a similar linear function. However, since the majority of the training time for the IF paradigm is spent on creating a pre-potency to respond (in the Go/No-go and the Stop task) or setting the stage for conflict resolution (Flanker task), only part of the time is spent on the actual key inhibitory component (as compared with 100% for the WM paradigm). Worth noting is that even though the IFs training showed a steady and significant improvement on two of the three training tasks (Go/No-go and Flanker), this improvement did not transfer to any of the non-trained measures of IF. This is quite striking as one of the trained tasks was essentially the same as the transfer test, i.e. the Go/No-go task. This implies that the increased training performance is task specific and involves superficial and non-transferable skill learning e.g. improved motor response coordination with regard to the location of the response keys on the keyboard, which differed in the tests.

One can also discuss whether these specific tasks are optimal for training or not. In the study by Davidson et al (2006) young children were able to inhibit a pre-potent response and uphold a decent level of performance even when switching rules between sets. However, when the rule switching trials were mixed within the same set, the younger age groups showed a disproportional decline in response inhibition performance. This proved much more difficult than when increasing the WM load. Perhaps using IFs tasks with concurrent switching would elicit better training effects of

IFs. An indication of this was found as an additional improvement for a switching training group compared to the Go/No-go training group on measures of response inhibition in a study by Dowsett and Lively (2000).

Other findings implicate contextual importance for development of IFs. In the preschool intervention program described by Diamond and colleagues (2007), the children trained IFs through dramatic play, taking turns listening/telling stories etc. IFs are thus trained in the situations where they are typically applied in everyday life. It may be that the situational context, integration with the environment and immediate application of IFs skills catalyze the training effects.

Finally, perhaps IFs are not developed enough to improve (with this type of intervention) at this age. An indication of this lies in the results showing larger improvements for the older children (4-5-year-olds compared with the 3-year-olds) after training on Go/No-go or switching tasks (Dowsett & Livesey, 2000) as well as improvements over test trials of response inhibition in 4-year-olds but not 3-year-olds (Carlson, et al. 2005). As dramatic improvements in IFs take place during these years, different samples of the same age ranges may show differential effects based on the large individual variation in this development.

On a different note, there may be some evolutionary reason for the delayed development of IFs as compared to for instance WM as recently discussed by Thompson-Schill (2009). She claims that immaturity of the IFs allow flexible thinking due to undeveloped control mechanisms which is essential for the development of other skills. She cautions that premature training of control processes may actually lead to non-exposure to potential learning situations. As the natural and normal variation in IFs is large in the preschool years, perhaps interventions should be held off until persistent impairments are more obvious.

5.3.4 Effects from NVR training

The results from Study IV showed that Gf can be improved in 4-year-olds with computerized training of NVR. Both the NVR and CB groups showed a significant improvement on the Gf latent variable whereas this was not the case for all of the tests when split into separate outcomes. Using the shared variance between NVR tasks assessing slightly different aspects contributes to reducing the measurement error, which is assumed to be unique in each task and thus not included in the latent variable. The fact that the NVR group but not the CB group showed improvement on Block design and Raven’s CPM Set B reinforces the importance of time spent on training. The CB group, which trained half the amount of time as the NVR group, did probably not receive enough training to show a significant effect compared to the control group on these tests (when assessed separately). However, the CB group improved just as much as (or even more than) the WM and NVR groups respectively on the trained tests (Grid task and Leiter). This means that even though improvements on a similar task is equivalent to the groups spending double the amount of time, the effects did not transfer as much to other non-trained tests (see Figure 2 in Study IV). This was illustrated with the regression analysis revealing interaction only for the trained tests, interpreted as an unexpected level of improvement on these tests given the reduced training time.

The only transfer effect *between* constructs was seen from NVR training to the Odd One Out. This indicates that the NVR training encompasses aspects of WM that are perhaps more related to processing of information as the Odd One Out has a higher load on this component than the Grid task does. This was observed in the pilot that preceded Study IV where the items in the training program were evaluated in terms of difficulty and compared to performance on Block design and the Grid task. The factors constituting the items were analyzed with multiple logistic regression models including interaction terms between the factors and Block design and Grid task. Results showed that increased load on a few of the factors were WM related. This type of manipulation was kept to a minimum since the training was meant to target NVR. Therefore the factors that increased difficulty in NVR-related way were primarily manipulated. However, WM components are always innate to NVR tasks and training is likely to have tapped WM to some degree. Gains in a visuospatial WM test were also reported in a recent study where a group training a wide range of commercially available NVR games outperformed a group training processing speed on this task (Mackey, 2010). This supports the hierarchical view of WM and NVR suggesting that WM is necessary to perform NVR tasks and may thus be secondarily affected when training a higher order cognitive function such as NVR. This could be discussed in relation to the finding that superior performance on a Raven’s APM task was associated with increased activity in brain areas (in the lateral prefrontal and parietal) during WM trials with a high load of interference exclusively (Gray, et al., 2003).

In opposition, it seems that (at least at this age and in typically developing samples) WM training does not extend to improvements in NVR. This may, however, occur when WM is a bottleneck for NVR performance, which is not likely the case in the samples studied here, but may have been the case in some of the previously reported instances studying ADHD samples (Klingberg, et al. 2002b; 2005). It could also mean that, in typically WM and NVR functioning individuals, a higher load on the processing component of WM training may be key to transfer to NVR, as seen in the studies by Jaeggi (2008; 2010).

5.3.5 Active control groups

As reported in the results section of Study IV, the non-significant effect on the word span test, led us to compare the pooled control groups from Study II and the WM training group from Study IV. In contrast to the PL comparison, these results showed that the training effect was significant. This raises the question of whether the PL group actually trained their WM and NVR to some degree as well. We consider the design of the study with regard to the active control group a strength of this study and feel confident that we controlled for nearly all other differences between groups. It is, however, possible that some of the true training effects in the other groups are undetected due to the strict nature of the control condition, thus eliciting a type II error. It is possible that repeatedly remembering the location of one stimulus throughout the whole training period actually trained WM to some degree. This was recently discussed in a WM training study including children with mild retardation (Van der Molen, Van Lult, Van der Molen, Klugkist, & Jongmans, 2010). They trained one group on an adaptive WM task (a version of the Odd One Out), one group on the same task but using a non-adaptive algorithm and a control group training on the perceptual aspect only (identification of the odd figure) in the task. The results showed that both WM training groups showed significant training effects 10 weeks after training on visual short-term memory, arithmetic and story recall compared to the control group. Even though this was a clinical sample, it is possible that that low load WM training may have beneficial effects in a typically developing population as well. Likewise for the NVR training paradigm, it may be that low level training, even on the most basic logical principles, elicits transferrable effects to non-trained NVR tasks to a small degree.

5.3.6 Prediction of transfer effects

The extent of transfer effects seen after training seems to differ between functions and it was discussed in Study IV that correlations between measures on the trained tasks and other functions at T1 do not offer sufficient predictive value of improvements of these functions. This was, however, only based on correlations of the limited number of transfer measures for each group in Study IV. This analysis was thus repeated, now including the pooled correlations between trained function and other functions at T1 for both Study II and IV (Figure 8). The average correlation between trained tasks (Go/No-go for IF training group, Leiter tests for NVR training group and CB group and Grid task or Corsi block tapping task for WM and CB training groups) and all of the available measures from the tests (listed in Figure 8) are plotted on the y-axis. This was then plotted against the standardized change post training on these measures. This only included transfer tests (within and between constructs) and no standardized change values of the “trained tests” (e.g. no value for the NVR training group on the Leiter tests was included and likewise between the WM training and the Grid task). There was no correlation between these variables (*r* = -0.03), indicating no apparent association between the degree of correlation between trained task and other tests at T1 and improvements seen on these tests at T2. In other words, this suggests that the level of correlation with the trained task at T1 does not correspond well with improvements seen on this test after training. This is somewhat puzzling and contra intuitive, however, this is only based on a few tests and averages between different training types and should thus be interpreted cautiously. This was, however, necessary to get enough data to perform (as somewhat) reliable correlation analysis. This means that it also includes the IF group which did not even show improvements on the so called trained test (Go/No-go), so the predicted transfer based on correlation with the trained task would be small.

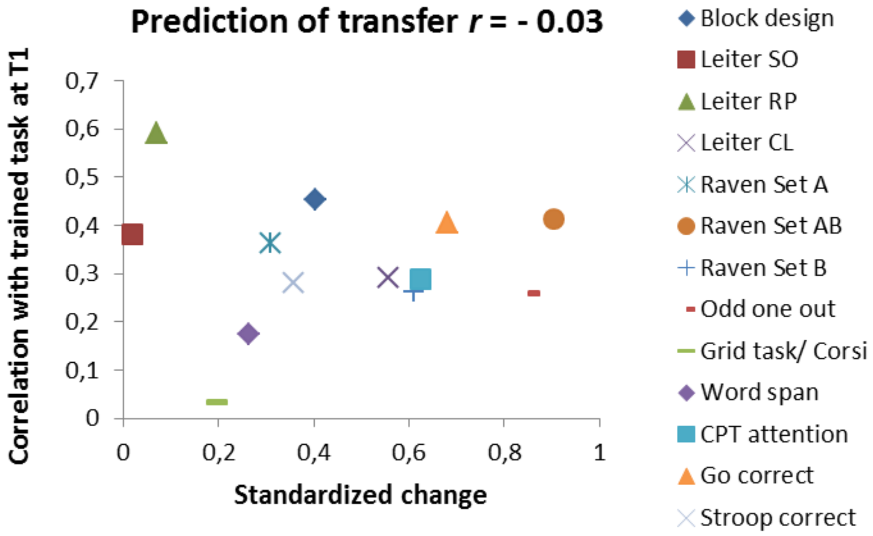


Figure 8. The y-axis shows the average correlations between the trained tasks (Go/No-go for IF training group, Leiter tests for NVR training group and CB group and Grid task or Corsi block tapping task for WM and CB training groups) and other test measures at T1. The x-axis shows the standardized change on these test measures after training. Only "real" transfer is included and the standardized change for trained tests are not included (i.e. the standardized change for the WM training groups to Grid task/Corsi are not included).

5.4 MUSIC TRAINING = COGNITIVE TRAINING? (STUDY V)

Cognitive training efforts have been developed based on laboratory measures of psychometric testing tools, with over all, in my opinion, promising results. It seems intuitive that tasks tapping a certain function, if repeated would elicit an improvement of the function tapped by it. However, there may be other, perhaps more natural ways to improve cognitive functioning. As described earlier, EFs are imperative to everyday functioning and are constantly more or less recruited. It then would seem natural that these daily cognitively challenging situations that result in EF recruitment would also help improve them. This is a question of nature versus nurture which is as endlessly interesting as it is complex. Studies on rats repeatedly report enhanced cognitive functioning in "enriched environment" conditions (for a review see Chapillon, Patin, Roy, Vincent, & Caston, 2002), which entails stimulating tools as well as constant physical optimization. Could daily engagement with certain stimulating tools or activities result in a type of cognitive training effects seen in intense targeted interventions? For instance, studies suggest that physical activity may lead to cognitive benefits (for a review see (Hillman, Erickson, & Kramer, 2008). Study V investigated the effects of music practice on cognitive development with similar findings.

The effects of music practice on WM and NVR were assessed with longitudinal neuropsychological measures and questionnaires on two occasions, two years apart, in a developing sample between the ages of 6 and 25. The results supported previous findings of association between music practice and superior WM and NVR performance (see Schellenberg, 2001 for a review). Our data also support the previously reported causal effects from music practice to cognitive benefits (Bugos, et al., 2007; Rauscher, et al., 1997; Schellenberg, 2004; Schlaug, Norton, Overy, & Winner, 2005). The novel findings in this study are the differential effect between WM and NVR in that WM improvement was best explained by the amount of music training per week and NVR improvements were better explained by the type of music practiced. This indicates that there is a dose-response effect for WM and perhaps a threshold effect for NVR. As illustrated in Figure 1 in Study V, the effects seem present already at T1 for the NVR domain even though this effect is more pronounced at T2. This indicates that the difference in performance between music categories is either there before they start playing an instrument or emerges quite rapidly after initiation. We did not find any explanation for differences between groups based on parental education level, sex, time spent on extracurricular hobbies or time spent on music practice in the two music groups. This does not mean that there aren't any alternative interpretations to our findings, but we did not find any other explanation in our data. The results on the visuospatial WM domain is perhaps more clear-cut showing a linear response to the time spent per week on music practice. However, the verbal WM domain did not show an effect of music practice. This is contradictive to previous findings showing both associations with (George & Coch, 2011; Lee, et al., 2007; Schellenberg, 2006), and causal effects of music practice to verbal WM (Bugos, et al., 2007). The raw scores (Table 2) suggest a superior performance for the group playing a "dual-staff instrument" however this effect is not significant. The reasons for this are unclear.

Another question examined was whether music practice acts directly on one of the two abilities (WM or NVR) and indirectly on the other (through mediation) or if there is a separate direct effect on each of them respectively. The results suggest that there is most likely a separate direct effect on each of the constructs, seen with a near significant music variable in the multiple linear regression analysis including the difference score of the other term. The final explanatory variables for WM performance at T2 were WM performance at T1 and hours of music practice per week. The variables best explaining NVR performance at T2 were NVR performance at T1, WM performance at T1, change in WM performance from T1 (T2-T1) and music category (based on dual-staff categorization). This suggests that there is a unidirectional dependency of NVR on WM, implying a hierarchical organization of the two functions.

One of the proposed underlying explanations for the effect of music practice on cognitive ability is the reading of musical notation. A recent study found that practice time explained 45% of the variance in sight reading, and that WM explained an additional 7% after controlling for practice time (Meinz & Hambrick, 2010). It is a complex process and has been showed to tap an integrated pattern of neural activity in the parietal and occipito-temporal cortex (Bengtsson & Ullen, 2006; Schon, et al., 2002; Stewart, et al., 2003). Even though we do not have data from our participants on sight reading ability, classifying the participants into groups based on the musical notation required for each instrument respectively elicits a better fit than when grouping them all together. Arguably, other factors could explain these better fitting groupings than musical notation category (single- or dual-staff), such as complexity of music style played, motor complexity of instrument or musical talent (regardless of time practiced). However, given the literature on neural activity and correlations between sight reading and WM and IQ respectively, the differences in cognitive development based on instrument played reported here, suggest musical notation as one candidate factor. Again, this cannot be deduced from our data and is thus just (an intriguing!) speculation at this point.

5.5 CONCLUDING REMARKS ON THE INTERRELATION BETWEEN HIGHER ORDER COGNITIVE ABILITIES

The findings from this thesis suggest that IFs and WM partly share common neural resources in adults. This does however, not mean that transfer will occur between the functions when trained (at least in preschool children). These results could also be interpreted as further support for the notion that different EFs develop at different rates and may consequentially be differently susceptible to training across ages. We have shown that visuospatial WM training improves not only storage components but also the central executive of WM, seen on a verbal short-term memory test and on a visuospatial WM test with higher processing demands than the trained tasks. We were not successful in improving IFs with training indicating either that IFs were not developed enough to train, or that this was done in a suboptimal way. We have however, shown that training of NVR improves Gf as a latent variable in preschoolers and transfers to a visuospatial WM task with a high processing load (Figure 9 for a theoretical account). We investigated whether training two related functions would have a synergistic effect and found no evidence of such an outcome. This is useful information to have when designing studies in the future. The finding that NVR training improved WM supports a hierarchical organization of NVR and WM, implying transfer of training effects from the top down but not from subsidiary functions upward. This may be different if WM capacity is a limitation for NVR performance. The hierarchical organization was also apparent in the music study where the final model explaining NVR performance included the WM variable as well, whereas NVR was not an explanatory variable in the best fitting model for WM performance. In summary, these results illustrate the complexity in the relations between these functions and offer some further information about factors determining transfer effects after training. I have attempted a schematic figure to summarize the possible theoretical framework for the findings in this thesis.

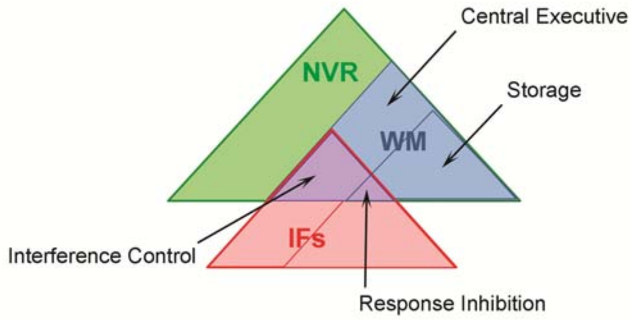


Figure 9. This is an attempt towards a schematic summary of the relations between NVR, WM and IFs based on the results from this thesis. It illustrates that WM is encompassed in NVR, explaining the training improvements in WM after NVR training. It also shows that WM and IFs are partly overlapping and in an attempt to adapt to variants of defining interference control, this part is set as overlapping with the central executive component of WM in particular. The hierarchical and mostly separate organization of WM and IFs explains why WM does not always transfer to IFs.

6 FUTURE DIRECTIONS

In retrospect, there are always ways in which you could have improved your studies in terms of control, design and execution to ensure that your conclusions are as substantiated as possible. Most often compromises are made to limit testing time, resources and practicalities allowing the actual completion of a study. Some of the unresolved questions from this thesis could perhaps have been answered if more tests were included in the training studies. This was, however, not possible due to risk for fatigue in the already long testing sessions. Furthermore, it would have been interesting to see how NVR training affects the brain and based on the effect on the Odd One Out, if the typical WM network would be affected similarly as with WM training. For the IF training study, it would be interesting to include older subjects in order to assess IFs in a population not undergoing the very basic and variable developmental stage that these children were in. Adjustment of the IF training tasks so that difficulty would be optimally adjusted as well as differentiating between response inhibition and interference control aspects of IF would be other steps to take. Naturally, follow up on cognitive training effects and scholastic performance would also be of importance and interest. Furthermore, clinical trials for both interventions on samples potentially benefiting from these types of remedies would be of utmost importance. The NVR training program has actually been piloted on a sample of children with mild retardation (IQ<70) with promising results (Söderqvist, Bergman Nutley, Ottersen, Grill, & Klingberg, 2011).

Regarding control conditions, it would have been interesting to include an additional active control group that did not train low load training of either WM or NVR, in order to assess the potential training effects of training with a low load paradigm. It is always the ambition to control for all of the non-active components (the active component presumed to be training at one's ability limit) in a treatment regime, however, there is a fine balance between a good control condition and one approximating training and thus type II errors (false negative findings) as there is some evidence that practice on the same tasks on low load, actually also improve performance on non-trained tasks (Van der Molen, et al., 2010). This would be good to investigate so that optimal control conditions can be designed and used in future studies allowing for sound conclusions to be drawn.

Regarding the unresolved questions from Study V, one would like to design a randomized, controlled intervention study directed at resolving the question of complexity in musical notation between instruments and its differential effects on NVR and WM. However, this, along with an endless sea of questions regarding the complexity of human cognitive functioning, is for future studies to resolve.

7 ACKNOWLEDGEMENTS

Enrolling in a PhD program is a very humbling experience and I am so grateful to have had the privilege to be surrounded by wise supervisors, stimulating and supportive colleagues and friends. I have many people to thank for their help and I will always be grateful to them and for circumstances enabling this immense learning experience.

Thank you…

To my main supervisor Torkel Klingberg who has provided me with guidance when I needed it and independence when I wanted it. It has been a true pleasure and inspiration to work with such a brilliant mind and I thank you for challenging me intellectually, creatively and personally. I also very much appreciate the many opportunities that you have generously enabled.

To my co-supervisor, Lisa Thorell for all your support. You have always tried to make yourself available to me when I have needed it.

To my confidant and colleague Stina Söderqvist for endless support, friendship and laughter. Your help with, just about everything, in Study III and IV has been invaluable and your generous spirit and personality has made my time here truly joyous.

To my former and current lab mates; Julian Macoveanu, Fredrik Edin, Fiona McNab, Gaëlle Leroux, Pernille Olesen, Fahime Darki, Iroise Dumontheil, Deepak Dash, Tim Ziermans, Chantal Roggeman and Heleen Feenstra for interesting discussions, distractions and shared digestives.

Da Brainchildz; Sara Bryde, Douglas Sjöwall, Ylva Samuelsson, Pelle Alexandersson, Stina Söderqvist for your excellent work in Study IV (and V) and for keeping the dream alive. Live tour in 2012.

To Sofia Lindqvist for an excellent collaboration in study II and pleasurable subsequent dinners (even those without rusty nails in our food…)

To Jonas Beckeman for your valuable solutions in programming the NVR training tasks and for an enjoyable collaboration. Thank you also to the rest of the team at Cogmed who have offered technical support and cognitive training expertise over the years.

To Keith Humphreys who has contributed statistical guidance in a very patient way. You are now subject to a saying often used in the lab: “what would Keith do…”

To Fredrik Strand for teaching me the ropes in Study I. Thank you for your patience.

To Ove Almqvist and Patrizia Vannini for giving me a good start in research.

To Fredrik Ullén for valuable discussions on the results in Study V.

To None-Marie Kemp and Louise von Essen for your much appreciated help with administration.

To my PhD and physics friends at the parking lot formerly known as MR-Centre; Karin, Bubben, Carolina, Kara, Valeria, Tina, Armita, Kattis, Örjan, Anke, Jonathan, Ulrika, Mattias, Magnus, Finn, Anders, Julia and Johanna. Thanks for the well needed breaks with fika moments, breakfasts, Lucia-tåg and lunches. Good times. Thank you also to the clinical staff at MRC, with a special shout out to Marie and Mimmi.

To the SBI-juniors for fun and interesting ski-conferences, pub-nights and workshops.

To my lunch posse from the research school: Ammi, Linda, Emma, Lena and Anna. Thank you for your stories, perspectives and company.

To Health Care Sciences Postgraduate School for financial aid and general support throughout my entire PhD-program. It has been a privilege to take part in the activities, courses and workshops organized for us and I am truly grateful for that.

To all of my subjects, their parents, preschool personnel and educators for your time, effort and enthusiasm.

To my mother in law, Gunilla, for your help with graphic design and Tom.

To Ambrosia, for energy boosts and creative outlet.

To all my wonderful friends (for reading at least this page…and) for perspective and laughter, for fika-moments, breakfasts at B&B, Thursday dinners and Bellman-nights. Love to you all.

To my parents for providing me with an enriched environment☺, and specifically to my father Ulf, for scientific inspiration, my mother Maj, for unconditional support and my sister Carin, for always believing in me.

To my little sun, Tom, for giving me perspective.

And most of all, thank you, Daniel. I couldn’t have done this without your support. Special thank you for your patience, your skilled management over my writing this thesis and for challenging “the divine truth”.

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